Initial REMS Approval: 10/2011
Most Recent Modification: 05/2015

BLA 125104

TYSABRI® (natalizumab) Intravenous Injection

Monoclonal Antibody

Biogen Idec, Inc
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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

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

Reference ID: 3753128

I. GOALS:

The goals of the Tysabri REMS are:

1. To inform prescribers, infusion center healthcare providers, and patients about the risk of progressive multifocal leukoencephalopathy (PML) associated with TYSABRI including the increased risk of PML with longer treatment duration, prior immunosuppressant use and the presence of anti-JCV antibodies.

2. To warn against concurrent use with antineoplastic, immunosuppressant, or immunomodulating agents, and in patients who are immunocompromised.

3. To promote early diagnosis of PML and timely discontinuation of TYSABRI in the event of suspected PML.

II. REMS ELEMENTS:

A. Medication Guide

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

Please see the appended Medication Guide.

B. Elements to Assure Safe Use

1. Healthcare providers who prescribe TYSABRI are specially certified.

a. Biogen Idec will ensure that health care providers who prescribe TYSABRI are specially certified.

b. To become certified, prescribers will be required to enroll in the TOUCH® Prescribing Program by completing the following requirements:

i. Review the TYSABRI REMS prescriber educational materials, including the full Prescribing Information.

ii. Complete and sign the Prescriber/Patient Enrollment Form and acknowledge the following:

a) I have read and understand the full Prescribing Information for TYSABRI

b) I understand that TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. When initiating and continuing treatment with

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

c) I am aware that cases of PML have been reported in patients taking TYSABRI who were recently or concomitantly treated with immunomodulators or immunosuppressants, as well as in patients receiving TYSABRI monotherapy

d) I understand that three risk factors identified thus far that increase the risk of PML in TYSABRI-treated patients are:

- Longer treatment duration, especially beyond 2 years
- Prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil)
- The presence of anti-JCV antibodies.

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

e) To my knowledge, this patient has no known contraindications to TYSABRI, including PML

f) I have instructed this patient to promptly report to me any new or worsening symptoms that persist over several days, especially nervous system symptoms

g) I understand that this patient should be seen and evaluated 3 months after the first infusion, 6 months after the first infusion, every 6 months thereafter for as long as this patient receives TYSABRI, and for at least 6 months after TYSABRI has been discontinued

h) I will determine every 6 months whether this patient should continue on TYSABRI and, if so, authorize treatment for another 6 months

i) 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.

j) I should report to Biogen Idec, as soon as possible, cases of PML, hospitalizations due to opportunistic infection, or deaths

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k) I understand that data concerning this patient and me will be entered into the mandatory TOUCH Prescribing Program. Biogen Idec 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

l) I have received educational materials regarding the benefits and risks of TYSABRI treatment

m) I have, or another healthcare provider under my direction has, educated this patient on the benefits and risks of treatment with TYSABRI, provided him or her with the Patient Medication Guide and Enrollment Form, instructed him or her to read these materials, and encouraged him or her to ask questions when considering TYSABRI

Acknowledgments specific to Multiple Sclerosis (MS)

I understand that TYSABRI is indicated as monotherapy for relapsing forms of MS

n) I understand that this patient has a relapsing form of MS based on clinical and radiological evidence

o) 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

p) 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

q) I understand that an MRI should be performed prior to initiating therapy with TYSABRI in MS patients

Acknowledgments specific to Crohn’s Disease (CD)

r) I understand that TYSABRI is indicated for adult patients with moderately to severely active CD with evidence of inflammation who have had an inadequate response to, or are

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unable to tolerate, conventional CD therapies and inhibitors of TNF-α

s) I understand that patients receiving TYSABRI should not take concomitant immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α

t) I understand that this patient has moderately to severely active CD with evidence of inflammation

u) I have discussed other Crohn's disease treatments with this patient

v) I understand that TYSABRI should be discontinued if a patient has not experienced a therapeutic benefit by 12 weeks of therapy

w) I understand that patients receiving steroid therapy at the time of TYSABRI initiation must undergo a steroid tapering regimen once a therapeutic response is achieved. If the patient with Crohn's disease cannot be tapered off of steroids within six months of starting TYSABRI, TYSABRI should be discontinued

c. Biogen Idec will:

i. Ensure that prescriber enrollment can successfully be completed

ii. Ensure that prescribers receive the TYSABRI prescribing information and the following materials that are part of the TYSABRI REMS and are appended:

- TOUCH Prescribing Program Educational Slide Set
- TOUCH Prescribing Program Enrollment Kits (specific to MS or CD)
    1. TOUCH Prescribing Program Overview
    2. Medication Guide
    3. Prescriber/Patient Enrollment Form (MS or CD)
    4. Pre-Infusion Patient Checklist (combined MS and CD)
    5. Guidance for Evaluation of New Neurologic Symptoms in Patients Receiving TYSABRI (MS)
    6. Understanding PML for Gastroenterologists (CD)
- TOUCH On-Line (www.TOUCHPROGRAM.com)
- Change Prescriber Authorization Form
- 12 Week Questionnaire for Crohn's Disease

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- Patient Status Report and Reauthorization Questionnaire (specific to MS and CD)
- Initial Discontinuation Questionnaire (specific to MS or CD)
- 6-Month Discontinuation Questionnaire (specific to MS or CD)

iii. Ensure that enrollment forms are complete before activating a prescriber's enrollment in the TOUCH Prescribing Program.

iv. Ensure that prescribers are notified when they are successfully enrolled in the TOUCH Prescribing Program, and therefore, are certified to prescribe TYSABRI.

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

a. Biogen Idec will ensure that certified pharmacies that dispense TYSABRI are specially certified.

b. Pharmacies that dispense TYSABRI to infusion sites must enroll in the Tysabri TOUCH Prescribing Program by submitting a completed enrollment form and designating a person with appropriate authority to acknowledge the following:

i. The pharmacy has received training and educational materials on the TOUCH Prescribing Program

ii. I understand that certified pharmacies may dispense TYSABRI only to authorized infusion sites

iii. I understand that, per the requirements of the TOUCH Prescribing Program, this certified pharmacy's compliance may be reviewed by the Food and Drug Administration (FDA) and/or audited by Biogen Idec and/or a third party designated by Biogen Idec.

I understand that noncompliance with the requirements of the TOUCH Prescribing Program may result in my pharmacy no longer being enrolled and termination of our participation in the program.

c. Biogen Idec will:

1. Ensure that pharmacies are notified when they are successfully enrolled in the TOUCH Prescribing Program, and therefore, are certified to dispense TYSABRI.

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2. Ensure that pharmacies that dispense TYSABRI to authorized infusion sites have been trained on the known risks, potential benefits, and appropriate use of TYSABRI using approved educational materials.

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

- TOUCH Prescribing Program Educational Slide Set
- TOUCH Prescribing Program Overview
- Certified Pharmacy Enrollment Form

e. Biogen Idec will ensure that infusion sites where TYSABRI is dispensed and administered are specially certified.

i. Infusion sites that dispense and administer TYSABRI must enroll in the TOUCH Prescribing Program by submitting a completed Infusion Site Enrollment Form and designating a person with appropriate authority to acknowledge the following:

a) The infusion site has received training and educational materials on the TOUCH Prescribing Program

1. I understand that TYSABRI will be administered only to patients who are currently authorized in the TOUCH Prescribing Program. Patient authorization must be confirmed *prior to each infusion* by*:*

1. For TOUCH On-Line infusion sites: Patient Authorization Status must be “Authorized” or
2. For paper-based infusion sites: Receipt of current Notice of Patient Authorization and verification that no Notice of Patient Discontinuation is on file

c) I understand that each patient will receive a copy of the TYSABRI Patient Medication Guide *prior to each infusion*

d) I understand that a TYSABRI Pre-infusion Patient Checklist must be completed *prior to each infusion*. The Pre-infusion Patient Checklist must be submitted to Biogen Idec within 1 business day of the patient visit, regardless of whether or not the patient received the infusion, by:

1. For paper-based infusion sites: sending a copy of the completed Pre-infusion Patient Checklist to Biogen Idec. A copy must also be placed in the patient’s medical record

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2. For TOUCH On-Line infusion sites: The infusion nurse can read, complete and submit the Pre-Infusion Patient Checklist directly in TOUCH On-Line

e) I understand that, per the requirements of the TOUCH Prescribing Program, this infusion site's compliance with the REMS may be reviewed by FDA and/or audited by Biogen Idec and/or a third party designated by Biogen Idec.

f) I understand that noncompliance with the requirements of the TOUCH Prescribing Program will result in de-enrollment of the infusion site.

f. Biogen Idec will:

i. Ensure that infusion sites are notified when they are successfully enrolled in the TYSABRI REMS Program, and therefore, are certified to dispense and administer TYSABRI.

ii. Ensure that infusion sites that dispense and administer TYSABRI have been trained on the known risks, potential benefits, and appropriate use of TYSABRI using approved educational materials.

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

- TOUCH Prescribing Program Educational Slide Set
- TOUCH Prescribing Program Overview
- Infusion Site Enrollment Form
- Pre-Infusion Patient Checklist
- Medication Guide

3. TYSABRI will be dispensed to patients with evidence or other documentation of safe-use conditions.

a. Biogen Idec will ensure that certified prescribers enroll all patients into the TOUCH Prescribing Program by completing the Prescriber/Patient Enrollment Form for each new patient.

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

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

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

a) This infection is called progressive multifocal leukoencephalopathy (PML). PML usually happens in people with weakened immune systems

b) There is no known treatment, prevention, or cure for PML

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

d) My chance for getting PML increases if I:
   a. Have received TYSABRI for a long time, especially longer than 2 years
   b. Have received certain medicines that can weaken my immune system before I start receiving TYSABRI
   c. 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

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

ii. Acknowledgments specific to MS

I understand that TYSABRI is a medicine approved to treat patients with relapsing forms of multiple sclerosis (MS)

a) TYSABRI increases the risk of PML. I understand that when starting and continuing treatment with TYSABRI, I should talk to

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my doctor about whether the expected benefit of TYSABRI is enough to outweigh this risk (see important information about PML below)

b) I have talked to my doctor and understand the benefits and risks of TYSABRI treatment

c) My chance for getting PML may be higher if I am also being treated with other medicines that can weaken my immune system, including other MS treatments. Even if I use TYSABRI alone to treat my MS, I can still get PML

iii. Acknowledgments specific to CD

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

a) I have talked to my doctor and understand the benefits and risks of TYSABRI treatment

b) I understand that I should not take certain medicines that weaken the immune system while I am taking TYSABRI

My chance for getting PML may be higher if I am also being treated with other medicines that can weaken my immune system, including other Crohn's disease treatments. Even if I use TYSABRI alone to treat my Crohn's disease, I can still get PML.

c. To receive TYSABRI all patients must be enrolled in a special program called the TOUCH Prescribing Program.

i. The TOUCH Prescribing Program is run by the company that makes TYSABRI. Under this program, the company is required to collect information about my health at regular time periods**. I cannot receive TYSABRI if I do not agree** to follow the requirements of the TOUCH Prescribing Program

ii. The company may use my information to meet the requirements of the TOUCH Prescribing Program, including helping me locate an authorized infusion site

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iii. I must notify the TOUCH Prescribing Program if I switch physicians or infusion sites

iv. I have received, read, and understand the Patient Medication Guide

v. I will bring to each TYSABRI infusion a list of all medicines and treatments that I have taken during the last month

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

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

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

C. Implementation System

The Implementation system for the TYSABRI REMS includes the following:

a. Biogen Idec must maintain a secure, validated database of all certified prescribers, certified pharmacies, certified infusion sites, and enrolled patients in the TOUCH Prescribing Program. The TOUCH Prescribing Program is an integrated, computerized, validated database that captures enrollment, patient tracking, and drug distribution data.

b. Biogen Idec will monitor the distribution of TYSABRI to ensure that the drug is only delivered to certified pharmacies and infused by certified infusion sites.

c. Biogen Idec will monitor the compliance of certified entities (i.e. pharmacies, infusion sites, and prescribers) as acknowledged in the signed entity specific enrollment form and, if appropriate, institute corrective actions, which could include retraining and de-enrollment

d. Biogen Idec will maintain TOUCH On-Line, which is an internet-based system that will allow enrolled TOUCH Prescribing Program participants the option of real-time access to view and/or submit required or pertinent patient therapy information collected through the TOUCH Prescribing Program, such as information on the Pre-infusion Patient Checklist, the TYSABRI Patient Status Report and Reauthorization Questionnaire, and the TYSABRI Patient Discontinuation Questionnaire.

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

D. Timetable for Submission of Assessments of the REMS

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

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Guidance for evaluation of new neurological symptoms in patients receiving TYSABRI

Please see accompanying full Prescribing Information, including Boxed Warning.

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Background information

Progressive multifocal leukoencephalopathy (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)

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

Please see accompanying full Prescribing Information, including Boxed Warning.

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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 Idec 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 Idec 6 months after initiating treatment and every 6 months thereafter, ensuring additional monitoring and reporting by Biogen Idec
- 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.

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.

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Evaluation of new neurological symptoms in patients receiving TYSABRI

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

Distinguishing PML from MS

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

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

	MS relapse	PML
ONSET	**Acute**	**Subacute**
EVOLUTION	➤ Over hours to days ➤ Normally stabilize ➤ Resolve spontaneously or with treatment	➤ Days to weeks ➤ Progressive
CLINICAL PRESENTATION	➤ Diplopia ➤ Paresthesia ➤ Paraparesis ➤ Optic neuritis ➤ Myelopathy	➤ Cortical symptoms/signs ➤ Behavioral and neuropsychological alteration ➤ Retrochiasmal visual deficits ➤ Seizures ➤ Hemiparesis

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

Please see accompanying full Prescribing Information, including Boxed Warning.

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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.

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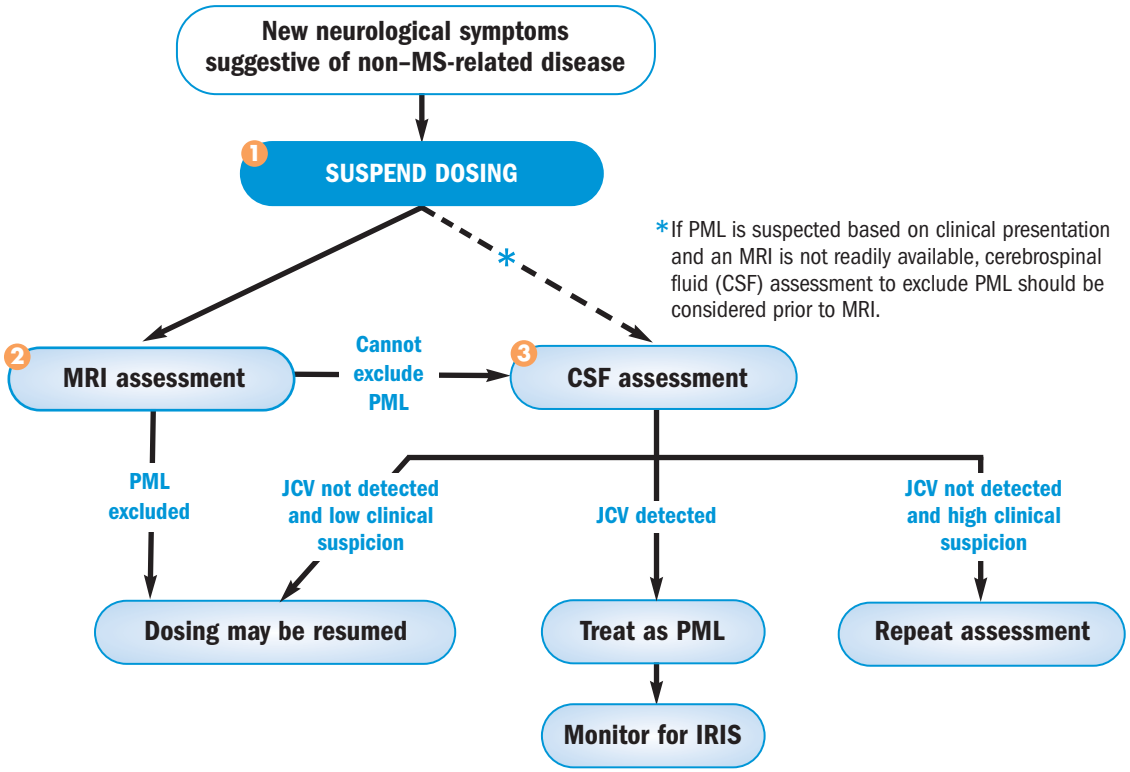
Suggested diagnostic algorithm for TYSABRI-treated patients experiencing new neurological symptoms suggestive of non–MS-related disease



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

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

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

Please see accompanying full Prescribing Information, including Boxed Warning.

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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 Idec at **1-800-456-2255**
  - Biogen Idec can provide additional resources, including suggested next steps

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.

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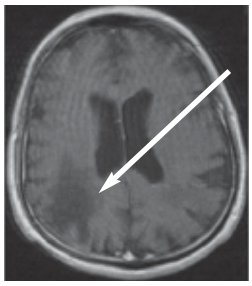
MRI assessment

- 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 5)
- 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

T1-weighted imaging	T2-weighted imaging
	
Large hypointense lesion in the region of the right occipital lobe (angular gyrus and intraparietal sulcus).	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.

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

Please see accompanying full Prescribing Information, including Boxed Warning.

Table 2. MRI lesion characteristics typical of PML and MS

Characteristic	MS Lesions	PML Lesions
Location	Periventricular perpendicular to ventricles (Dawson's fingers), deep white matter, isolated U fibers, cerebellum and spinal cord	➤ Subcortical WM in parietal, occipital or frontal lobes ➤ May involve precentral or postcentral gyrus (motor/sensory cortex) or insular region ➤ Follows WM tracks. Can cross the corpus callosum to contralateral hemisphere (butterfly pattern) or extend through internal capsule ➤ Rarely brainstem or cerebellar WM ➤ No spinal cord involvement
Appearance	Well defined borders	➤ Infiltrating, ill-defined, confluent WM lesions which can be multifocal
Mass effect	Large lesions can have a mass effect	➤ Rare even in large lesions
FLAIR	Flair = T2	➤ Flair more sensitive for detection of PML lesions in subcortical location
T1W pre-contrast	Isotense or mildly hypointense to Grey matter	➤ Isointense with progressive hypointensity
T1 post contrast	Homogeneous or ring-enhancement – resolves in 1-2 months	➤ Patchy, punctate or linear

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

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.

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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 plasma exchange has not been 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

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

Please see accompanying full Prescribing Information, including Boxed Warning.

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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 Idec 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

Mail: Biogen Idec Medical Information
14 Cambridge Center
Cambridge, MA 02142

Web: http://medinfo.biogenidec.com

E-mail: medinfo@biogenidec.com

To report an adverse event, contact:

Biogen Idec

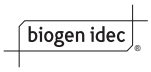
Telephone: 1-800-456-2255

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.

TYSABRI® (natalizumab)

Reference ID: 3753128

Please see accompanying full Prescribing Information, including Boxed Warning.



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Reference ID: 3753128

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

Prescriber/Patient Enrollment Form—MS

Completion of all pages is required.

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

Patient Information

Date of b rth _____ / _____ / _____
(MM/DD/YYYY)

Pat ent name _____ ____ _____
F rst M Last

Street address _____

C ty_____ State_____ Z P_____

Work te ephone ☐☐☐-☐☐☐-☐☐☐☐

Home te ephone ☐☐☐-☐☐☐-☐☐☐☐

Pat ent may be contacted at ☐ Home ☐ Work Best t me _____

Fema e ☐ Ma e ☐ _____
E-ma address

Insurance Information

Pat ent SSN ☐☐☐-☐☐-☐☐☐☐

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

☐ Check f no nsurance ☐ Med care ☐ Med ca d _____
Med ca d P an Type

Po cyho der s name _____ ____ _____
F rst M Last

_____ _____
Pr mary nsurance nsurance company te ephone

_____ _____
Po cy number Group number

_____
Pharmacy benef t 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 Idec 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 Idec Inc. 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 Idec 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 Idec 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 Idec, federal privacy laws may no longer protect the information. However, Biogen Idec 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 Idec 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 Idec 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 relapsing forms of multiple sclerosis (MS).

- 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 this risk (see important information about PML below).

Initials:_____

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

- This infection is called progressive multifocal leukoencephalopathy (PML). PML usually happens in people with weakened immune systems
- There is no known treatment, prevention, or cure for PML
- My chance for getting PML may be higher if I am also being treated with other medicines that can weaken my immune system, including other MS treatments. Even if I use TYSABRI alone to treat my MS, I can still get PML
- My chance for getting PML increases if I:
  - Have 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
  - 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

  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: _____/_____/_____
F rst M Last (MM/DD/YYYY)

Patient signature (or personal representative): _____ Date: _____

Authority of personal representative (*if applicable*): _____

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

Prescriber/Patient Enrollment Form—MS

Completion of all pages is required.

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

Patient History

at ent name: _____ ___ _____ DOB: ____/____/____
F rst MI Last (MM/DD/YYYY)

Date of f rst symptoms: ____/____/____
(MM/DD/YYYY)

ease nd cate the pat ent's **MOST ReCeNT** therapy for (f pat ent was most recent y on comb nat on therapy, check a that app y). None ☐

A ONEx® ☐ PLEGRIDY ☐ Betaseron® ☐ Copaxone® ☐ eb f® ☐ YSABRI® ☐ Extav a® ☐ G enya™ ☐

TECFIDERA® ☐ Aubag o® ☐ LEMTRADA™ ☐ Azath opr ne ☐ Methotrexate ☐ toxantrone ☐ Mycopheno ate ☐

Cyc ophospham de ☐ Other ☐

ease nd cate the start and stop dates of most recent therapy: Start date ☐☐/☐☐☐☐ (Y Y Y Y) Stop date ☐☐/☐☐☐☐ (Y Y Y Y)

Has the pat ent ever rece ved YSABRI before? Yes ☐ No ☐

Has the pat ent **eVeR** been prescr bed an mmunosuppressant or an ant neop ast c therapy for any cond t on? Yes ☐ No ☐

If yes, p ease check a of the fo ow ng that app y:

Azath opr ne ☐ Cyc ophospham de ☐ Methotrexate ☐ toxantrone ☐ Mycopheno ate ☐ Other ☐

Has the pat ent **eVeR** been tested for the presence of ant -JCv ant bod es? Yes ☐ No ☐ nknown ☐

If yes, has the pat ent **eVeR** tested **POSfTfVe** for the presence of ant -JCv ant bod es? Yes ☐ No ☐ end ng ☐

Prescription for TYSABRI

Dose: TYSABRf® (natalizumab) 300 mg **Dispense: 1 vial** **Refills: 12** **Directions: fV infusion per Prescribing fnformation every 4 weeks**

I author ze B ogen Idec as my des gnated agent and on beha f of my pat ent to (1) use the nformat on on th s form to enro the above-named pat ent n the OUCH Prescr b ng Program, (2) furn sh any nformat on on th s form to the nsurer of the above-named pat ent, (3) forward the nformat on on th s form to the prescr ber or nfus on s te adm n ster ng YSABRI, f app cab e, (4) forward the above prescr pt on by fax or by another mode of de very to a pharmacy, f app cab e, and (5) coord nate de very of YSABRI on beha f of the above-named pat ent.

Prescriber signature (stamps not acceptab e):_____ Date:_____

Prescriber

Prescr ber name: _____ ___ _____ _____
First MI Last Off ce contact

_____ _____
Street address ax ID #

_____ _____ _____ _____
C ty State ZIP DEA #

e ephone ☐☐☐-☐☐☐-☐☐☐☐ _____
Fax ☐☐☐-☐☐☐-☐☐☐☐ NPI/UPIN/prov der ID # w th pat ent's nsurer(s)

Continued on next page

Prescriber Acknowledgment

- I have read and understand the full Prescribing Information for TYSABRI
- I understand that TYSABRI is indicated as monotherapy for relapsing forms of MS
- 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 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 immunosuppresants, 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:
  - Longer treatment duration, especially beyond 2 years
  - Prior treatment with an immunosuppressant (e.g.,mitoxantrone, azathioprine, methotrexate, cyclophosphsmide, mycophenolate mofetil)
  - The presence of anti JCV antibodies

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

Patient name: _____ ___ _____ Date of birth: _____/_____/_____
First M Last (MM/DD/YYYY)

Prescriber signature: _____ Date: _____

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

Prescriber/Patient Enrollment Form—MS

Completion of all pages is required.

Please bmit this f o:
Biogen Idec
www.touchprogram.com
Fax: 1-800-840-1278

Patient Information

Date of b rth _____ / _____ / _____ (MM/DD/YYYY) Pat ent name _____ F rst ____ M _____ Last

In add t on, I a ow the shar ng of my hea th nformat on to the person or peop e I name be ow. B ogen Idec may contact the peop e named be ow to d scuss my enro ment n the TOUCH Program.

Designated Individual (pr nt name): Relationship:

Infusion Site Information*

1 **Prescriber ad er TYSABRI** and request the fo ow ng serv ces (check on y one):

☐ No serv ces requ red **OR** ☐ Forward th s prescr pt on to a spec a ty pharmacy prov der to nvest gate pharmacy coverage and coord nate de very to prescr ber's off ce **OR** ☐ P ease conduct nsurance research and procurement opt ons for TYSABRI

OR

2 **P e c be efe TYSABRI ea e a he e** (check on y one):

☐ I requ re ass stance n ocat ng an nfus on s te **OR** ☐ I am referr ng the pat ent to the fo ow ng nfus on s te or hea thcare prov der:

Name of adm n ster ng hea thcare prov der (f rst, ast) _____

Off ce contact _____

S te name _____

Te ephone ☐☐☐-☐☐☐-☐☐☐☐

Street address or s te Author zat on Number _____

Fax ☐☐☐-☐☐☐-☐☐☐☐

C ty _____ State _____ ZIP _____

*Note: TYSABRI can on y be nfused at author zed nfus on s tes. B ogen Idec w contact you f the nfus on s te you have nd cated s not author zed to nfuse TYSABRI.

Please see accompa ying fu Prescribing Informa ion, including Bo ed Warning, f a safet information.

biogen idec®

A o e ade a ks a e e a ks of e espec ve ow e s.

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TYSABRI® (natalizumab)

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

TYSABRI Patient Status Report and Reauthorization Questionnaire—MS

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

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

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

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

A Is the patient still under <MD name>'s care?
☐ Yes ☐ No/I don't know

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

_____

B Is the patient alive?
☐ Yes ☐ No

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

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

D **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, test result:
☐ Positive ☐ Negative ☐ Pending

G Is the patient currently receiving or has the patient received intermittent courses of steroids for the treatment of MS relapse in the previous 6 months?
☐ Yes ☐ No

If Yes, please circle the number of courses received.
1 2 3 4 5 6 >6

H Is the patient currently receiving or has the patient received any **IMMUNOMODULATORY** or **IMMUNOSUPPRESSANT** products in the previous 6 months?
☐ Yes ☐ No

If Yes, please indicate the type of therapy and number of months of use.

	Months of Use in Last 6 Months					
AVONEX®	1	2	3	4	5	6
Betaseron®	1	2	3	4	5	6
Copaxone®	1	2	3	4	5	6
Rebif®	1	2	3	4	5	6
Extavia®	1	2	3	4	5	6
Gilenya™	1	2	3	4	5	6
Aubagio®	1	2	3	4	5	6
PLEGRIDY™	1	2	3	4	5	6
TECFIDERA®	1	2	3	4	5	6
LEMTRADA™	1	2	3	4	5	6
Azathioprine	1	2	3	4	5	6
Methotrexate	1	2	3	4	5	6
Mitoxantrone	1	2	3	4	5	6
Mycophenolate	1	2	3	4	5	6
Cyclophosphamide	1	2	3	4	5	6
Chronic systemic steroids	1	2	3	4	5	6
Other immunomodulatory or immunosuppressant therapy	1	2	3	4	5	6

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 Idec 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).

Prescriber signature: _____ Date (MM/DD/YYYY): _____ /_____ /_____

(If applicable) Print TOUCH Authorized Prescriber Delegate Name : _____

_____

Please Note: A TOUCH authorized physician may complete this form on behalf of the Prescriber of record. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient and with HIPAA and applicable privacy rules.
If you have questions, or if you need additional information, please call 1-800-456-2255 from 8:30 AM to 8:00PM (ET).

Please see full Prescribing Information, including Boxed Warning, at www.TYSABRI.com

biogen idec®

TYSABRI® (natalizumab)

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

TYSABRI Initial Discontinuation Questionnaire—MS

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

Prescriber name: _____ ___ _____
First MI Last

Prescriber address: _____ _____ _____ _____
City State ZIP

Patient: _____ ___ _____ Patient Enrollment Number: _____
First name MI Last name

Patient date of birth (MM/DD/YYYY): _____/_____/_____

- This TYSABRI Patient Discontinuation Questionnaire is necessary to fulfill the tracking requirements of the TOUCH Prescribing Program for all patients treated with TYSABRI. You may also be contacted for additional information in response to answers provided on this form
- Submit the completed TYSABRI Patient Discontinuation Questionnaire to Biogen Idec 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 Idec:

C **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

*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).

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

☐ Yes ☐ Not performed

If performed, test result:

☐ Positive ☐ Negative ☐ Pending

Prescriber signature: _____ Date (MM/DD/YYYY): _____ /_____ /_____

(If applicable) Print TOUCH Authorized Prescriber Delegate Name: _____

Please Note: A TOUCH authorized physician may complete this form on behalf of the Prescriber of record. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient and with HIPAA and applicable privacy rules. If you have questions, or if you need additional information, please call 1-800-456-2255 from 8:30 AM to 8:00 PM (ET).

Please see full Prescribing Information, including Boxed Warning, at www.TYSABRI.com

biogen idec®

TYSABRI® (natalizumab)

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mm/yy
3-7428-XX

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

TYSABRI 6-Month Discontinuation Questionnaire—MS

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

Prescriber name: _____ ___ _____
First MI Last

Prescriber address: _____ _____ _____ _____
City State ZIP

Patient: _____ ___ _____ Patient Enrollment Number: _____
First name MI Last name

Patient date of birth (MM/DD/YYYY): _____/_____/_____

- This TYSABRI Patient Discontinuation Questionnaire is necessary to fulfill the tracking requirements of the TOUCH Prescribing Program for all patients treated with TYSABRI. You may also be contacted for additional information in response to answers provided on this form
- Submit the completed TYSABRI Patient Discontinuation Questionnaire to Biogen Idec 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 Idec:

C **PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)**

☐ Yes ☐ No or ☐ Under investigation

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

☐ Yes ☐ No or ☐ Under investigation

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

E **MALIGNANCY**

☐ Yes ☐ No or ☐ Under investigation

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

☐ Yes ☐ Not performed

If performed, test result:

☐ Positive ☐ Negative ☐ Pending

Prescriber signature: _____ Date (MM/DD/YYYY): _____ /_____ /_____

(If applicable) Print TOUCH Authorized Prescriber Delegate Name: _____

Please Note: A TOUCH authorized physician may complete this form on behalf of the Prescriber of record. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient and with HIPAA and applicable privacy rules.
If you have questions, or if you need additional information, please call 1-800-456-2255 from 8:30 AM to 8:00PM (ET).

Please see full Prescribing Information, including Boxed Warning, at www.TYSABRI.com

biogen idec®

TYSABRI® (natalizumab)

Understanding PML for Gastroenterologists

TYSABRI®
(natalizumab)

Reference ID: 3753128

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 include[3,4]:

- 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]

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.

TYSABRI® (natalizumab)

Reference ID: 3753128

Action Steps if PML Is Suspected

- TYSABRI dosing should be suspended immediately in all cases in which PML is suspected[1]
- Immediate referral to a neurologist for assessment, potentially including[1]:

  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 Idec 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

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 duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. 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

TYSABRI®
(natalizumab)

Important Safety Information (continued)

Progressive Multifocal Leukoencephalopathy (PML)

- Infection by the JC Virus is required for the development of PML.
- Anti-JCV antibody testing should not be used to diagnose PML.
- 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.
- PML has been reported following 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 six months following discontinuation of TYSABRI.
- In MS patients, an MRI scan should be obtained prior to initiating therapy with TYSABRI. This MRI may be helpful in differentiating subsequent multiple sclerosis symptoms from PML.
- Three sessions of plasma exchange 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 which may occur during plasma exchange include clearance of other medications and volume shifts, which have the potential to lead to hypotension or pulmonary edema. Although plasma exchange has not been 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.
- Anti-JCV antibody testing should not be performed during or for at least two weeks following plasma exchange due to the removal of antibodies from the serum.
- 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

TYSABRI® (natalizumab)

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 full 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 Idec 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 Idec at 1-800-456-2255 and to the Food and Drug Administration's MedWatch Program at 1-800-FDA-1088 as soon as possible.

Important Safety Information Continued on next page

TYSABRI® (natalizumab)

- 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.

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, TYSBARI should be discontinued, and appropriate treatment for herpes encephalitis/meningitis should be administered.

Hepatotoxicity

- Clinically significant liver injury, including acute liver failure requiring transplant, has been reported in patients treated with TYSABRI in the postmarketing setting. In some patients, liver injury recurred upon rechallenge, providing evidence that TYSABRI caused the injury.
- 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).

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%.

Important Safety Information Continued on next page

TYSABRI® (natalizumab)

- 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 to patients who did not develop antibodies to TYSABRI in both MS and CD studies.
- Patients who receive TYSABRI after an extended period without treatment may be at higher risk of hypersensitivity reactions.

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 Study MS1 and Study 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.

Important Safety Information Continued on next page

TYSABRI® (natalizumab)

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 that are frequently transient.

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% versus 0.3%) and pneumonia (0.6% versus 0%), acute hypersensitivity reactions (1.1% vs 0.3%, including anaphylaxis/anaphylactoid reaction [0.8% versus 0%]), depression (1.0% vs 1.0%, including suicidal ideation or attempt [0.6% versus 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.

TYSABRI®
(natalizumab)

References:
1. TYSABR prescribing informa ion. Cambridge, MA: Biogen dec. **2.** Yousry TA, Major EO, Ryschkewi sch C, e al. Evalua ion of pa ien s rea ed wi h na alizumab for progressive mul ifocal leukoencephalopa hy. *N Engl J Med.* 2006;354:924-933. **3.** Da a on file. Cambridge, MA: Biogen dec. **4.** Projec nform. Progressive mul ifocal leukoencephalopa hy (PML). Available a : h p://www.projec inform.org/info/pml/index.sh ml. Accessed ebruary 14, 2008.

Please see accompanying full Prescribing Information, including Boxed Warning.

biogen idec®

TYSABRI®
(natalizumab)

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Reference ID: 3753128

CD TouCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health
Phone 1 800 456 2255

Prescriber/Patient Enrollment Form—Crohn's Disease

Completion of all pages is required.

lease submit this form to:
B ogen dec
www.touchprogram.com
ax: 1 800 840 1278

Patient Information

Date of b rth _____ / _____ / _____
(MM/DD/YYYY)

Pat ent name: _____ ____ _____
rst M Last

Street address

C ty State Z P

Work te ephone ☐☐☐-☐☐☐-☐☐☐☐

Home te ephone ☐☐☐-☐☐☐-☐☐☐☐

Pat ent may be contacted at ☐ Home ☐ Work Best t me _____

Fema e ☐ Ma e ☐

E-ma address

Insurance Information

Pat ent SSN ☐☐☐-☐☐-☐☐☐☐

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

☐ Check f no nsurance ☐ Med care ☐ Med ca d _____
Med ca d P an Type

Po cyho der s name _____ ____ _____
rst M Last

Pr mary nsurance

nsurance company te ephone

Po cy number

Group number

Pharmacy benef t 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 Idec 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 Idec Inc. 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 Idec 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 Idec 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 Idec, federal privacy laws may no longer protect the information. However, Biogen Idec 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 Idec 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.

atient signature (or personal representative): _____ Date: _____

Authority of personal representative (*if applicable*): _____

Prescriber/Patient Enrollment Form—Crohn's Disease

Completion of all pages is required.

lease submit this form to:
B ogen dec
www.touchprogram.com
ax: 1 800 840 1278

Patient Acknowledgment

Biogen Idec 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.

understand that ABRI 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

nitials:_____

understand that ABRI 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 Crohn's disease treatments. Even if I use TYSABRI alone to treat my CD, I can still get PML
- My chance for getting PML increases if I:
  - 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
  - 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.

  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

nitials:_____

o receive ABRI, all patients must be enrolled in a restricted program called the TOUCH rescribing rogram.

- 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. **cannot receive ABRI if 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

nitials:_____

atient name: _____ _____ _____ Date of birth: _____/_____/_____
F rst M Last (MM/DD/YYYY)

atient signature (or personal representative): _____ Date: _____

Authority of personal representative (*if applicable*): _____

CD TouCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health
Phone 1 800 456 2255

Prescriber/Patient Enrollment Form—Crohn's Disease

Completion of all pages is required.

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

Patient History

Patient name: _____ ____ _____ DOB: ____/____/____
rst M Last (MM/DD/YYYY)

Date of first Crohn's disease symptoms: _____
(MM/YYYY)

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

Med cat on	Ongo ng	OR	Stopped	Med cat on	Ongo ng	OR	Stopped
☐ None				Methotrexate	☐		☐
Rem cade®	☐		☐	System c stero ds	☐		☐
Hum ra®	☐		☐	Entyv o M	☐		☐
Azath opr ne or Mercaptopur ne or Th oguan ne	☐		☐	Other mmunomodu atory therapy or mmunosuppressant therapy (not nc ud ng am nosa cy ates)	☐		☐
C mz a®	☐		☐				

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 of the following that apply:

Remicade ☐ Humira ☐ Azathioprine or Mercaptopurine or Thioguanine ☐ C mz a ☐ Methotrexate ☐

Systemic steroids ☐ Vedolizumab (Entivio™) Other ☐

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

If yes, has the patient **eVeR** tested **Ve** for the presence of anti-JCV antibodies? Yes ☐ No ☐ Pending ☐

Prescription for TYSABRI

Dose: ABRI® (natalizumab) 300 mg Dispense: 1 vial efills: 12 Directions: infusion per rescribing Information every 4 weeks

I authorize Biogen Idec 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.

rescriber signature (stamps not acceptable): Date:

Prescriber

Prescriber name: _____ ____ _____
rst M Last

Off ce contact

Street address

Tax D #

C ty State Z P

DEA #

Te ephone ☐☐☐-☐☐☐-☐☐☐☐

Fax ☐☐☐-☐☐☐-☐☐☐☐

NP /UP N/prov der D # w th pat ent's nsurer(s)

Continued on next page

Prescriber/Patient Enrollment Form—Crohn's Disease

Completion of all pages is required.

lease submit this form to:
B ogen dec
www.touchprogram.com
ax: 1 800 840 1278

Prescriber Acknowledgment

- I have read and understand the full 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 immunosuppresants, 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:
  - -Longer treatment duration, especially beyond 2 years
  - -Prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil)
  - -The presence of anti-JCV antibodies

  These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI
- 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 Idec
- I understand that data concerning this patient and me will be entered into the mandatory TOUCH Prescribing Program. Biogen Idec 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

atient name: _____ ____ _____ Date of birth: _____/_____/_____
rst M Last (MM/DD/YYYY)

rescriber signature: _____ Date: _____

CD TouCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health
Phone 1 800 456 2255

Prescriber/Patient Enrollment Form—Crohn's Disease

Completion of all pages is required.

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

Patient Information

Date of b rth _____ / _____ / _____ (MM/DD/YYYY) Pat ent name _____ F rst ____ M _____ Last

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

Designated Individual (print name): Relationship:

Infusion Site Information*

1 **rescriber will administer ABRI** 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 **rescriber will refer AB 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 nfus on s te or hea thcare prov der (f rst ast)

Street address or S te Author zat on Number

C ty State Z P

Off ce contact

Te ephone ☐☐☐-☐☐☐-☐☐☐☐

Fax ☐☐☐-☐☐☐-☐☐☐☐

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

lease see accompanying full rescribing nformation, including Boxed arning, for important safety information.

biogen idec®

A o e ade a ks a e e a ks of e espec ve ow e s.

TYSABRI® (natalizumab)

– 2008 2013 B ogen dec /yy

4-7002-xx

Reference ID: 3753128

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

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

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

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

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

Dear <MD Name>,

Our records indicate that <Patient Name>'s authorization to receive TYSABRI will expire on <MM/DD/YYYY> and he/she will no longer be able to receive TYSABRI. Please submit the completed form to Biogen Idec 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 Idec:

C **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, test result:
☐ Positive ☐ Negative ☐ Pending

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

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

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

	Months of Use in Last 6 Months					
Remicade®	1	2	3	4	5	6
Humira®	1	2	3	4	5	6
Azathioprine or Mercaptopurine or Thioguanine	1	2	3	4	5	6
Vedolizumab (Entivio™)	1	2	3	4	5	6
Methotrexate	1	2	3	4	5	6
Cimzia®	1	2	3	4	5	6
Other immunomodulatory or immunosuppressant therapy†	1	2	3	4	5	6

†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 Idec 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).

Prescriber signature: _____ Date (MM/DD/YYYY): _____ /_____ /_____

(If applicable) Print TOUCH Authorized Prescriber Delegate Name: _____

Please Note: A TOUCH authorized physician may complete this form on behalf of the Prescriber of record. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient and with HIPAA and applicable privacy rules.
If you have questions, or if you need additional information, please call 1-800-456-2255 from 8:30 AM to 8:00 PM (ET).

Please see full Prescribing Information, including Boxed Warning, at www.TYSABRI.com

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4-7001-xx

TYSABRI® (natalizumab)

Reference ID: 3753128

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

TYSABRI 12-Week Questionaire for Crohn's Disease

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

<Date>

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

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

Dear <Prescriber Name>,

Our records indicate that it has been 12 weeks since <Patient Name> received his or her first dose of TYSABRI. The Prescribing Information states that if a patient with Crohn's disease has not experienced a therapeutic benefit by 12 weeks of induction of therapy she/he should be discontinued from TYSABRI treatment.

This 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 evaluation to Biogen Idec via TOUCH On-Line (www.touchprogram.com) OR fax (1-800-840-1278) and place one copy in the patient's record.

Please answer Yes or No to the following questions:

1. **Has this patient experienced a therapeutic benefit within 12 weeks after starting TYSABRI treatment?**

   ☐ Yes ☐ No*

   *TYSABRI should be discontinued if the patient has not experienced a therapeutic benefit by 12 weeks of induction therapy with TYSABRI.

2. **Will the patient continue on TYSABRI?**

   ☐ Yes ☐ No*

   *If you answer **No**, Biogen Idec 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 discontinuation questionnaire to complete for this patient.

If you have questions, or if you need additional information, please call 1-800-456-2255 from 8:30AM to 8:00PM (ET).

Prescriber signature: _____ Date (MM/DD/YYYY): _____/_____/_____

(If applicable) Print TOUCH Authorized Prescriber Delegate Name: _____

Please Note: A TOUCH authorized physician may complete this form on behalf of the TOUCH Prescriber of record. This questionnaire will be used consistent with the TOUCH Prescr ber/Patient Enrollment form signed by you and your patient with HIPAA and applicable privacy rules.

For full Prescribing Information, including Boxed Warning, please see www.TYSABRI.com.

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TYSABRI (natalizumab)

Reference ID: 3753128 © 2008-2013 Biogen Idec

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

TYSABRI Initial Discontinuation Questionnaire—Crohn's Disease

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

<Date>

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

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

Dear <MD Name>,

Our records indicate that <Patient Name> received a final dose of TYSABRI on <MM/DD/YYYY> . You may receive this questionnaire twice, once at discontinuation and a second time 6 months later.

- This Initial Discontinuation Questionnaire is necessary to fulfill the tracking requirements of the TOUCH Prescribing Program for Crohn's disease patients treated with TYSABRI. You may also be contacted for additional information in response to answers provided on this form.
- Submit the completed Initial Discontinuation Questionnaire to Biogen Idec 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 Idec:

C **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, test result:
☐ Positive ☐ Negative ☐ Pending

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 and the number of months of use.

	Months of Use in Last 6 Months					
Remicade®	1	2	3	4	5	6
Humira®	1	2	3	4	5	6
Azathioprine or Mercaptopurine or Thioguanine	1	2	3	4	5	6
Vedolizumab (Entyvio ™)	1	2	3	4	5	6
Methotrexate	1	2	3	4	5	6
Cimzia®	1	2	3	4	5	6
Other immunomodulatory or immunosuppressant therapy†	1	2	3	4	5	6

†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).

Prescriber signature: _____ Date (MM/DD/YYYY): _____ /_____ /_____

(If applicable) Print TOUCH Authorized Prescriber Delegate Name: _____

Please Note: A TOUCH authorized physician may complete this form on behalf of the Prescriber of record. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient and with HIPAA and applicable privacy rules.
If you have questions, or if you need additional information, please call 1-800-456-2255 from 8:30 AM to 8:00 PM (ET).

Please see full Prescribing Information, including Boxed Warning, at www.TYSABRI.com

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4-7004-XX

Reference ID: 3753128

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

TYSABRI 6-Month Discontinuation Questionnaire–Crohn's Disease

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

<Date>

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

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

Dear <Prescriber Name>,

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

- This Discontinuation Questionnaire is necessary to fulfill the tracking requirements of the TOUCH Prescribing Program for Crohn's disease patients treated with TYSABRI. You may also be contacted for additional information in response to answers provided on this form.
- Submit the completed 6-Month Discontinuation Questionnaire to Biogen Idec 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 Idec:

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

***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).

Prescriber signature: _____ Date (MM/DD/YYYY): _____/_____/_____

(If applicable) Print TOUCH Authorized Prescriber Delegate Name: _____

Please Note: A TOUCH authorized physician may complete this form on behalf of the TOUCH Prescriber of record. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient and with HIPAA and applicable privacy rules. If you have questions, or if you need additional information, please call 1-800-456-2255 from 8:30 AM to 8:00 PM (ET).

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TOUCH PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Biogen Idec
Fax: 1-800-840-1278
Phone: 1-800-456-2255

By Facsimile

Change Prescriber Authorization

PRESCRIBER AUTHORIZATION REQUESTED

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

Our records indicate that <Pat_First_Name> <Pat_Last_Name> will continue his/her TYSABRI (natalizumab) therapy under your care. If you agree to accept this patient, please sign this form and fax it to Biogen Idec 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, 8:30 AM to 8:00 PM (ET).

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 Idec 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

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TYSABRI (natalizumab)

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3-3060-xx

Reference ID: 3753128

TOUCH® PRESCRIBING PROGRAM

TYSABRI Outreach: Unified Commitment to Health

Phone: 1-800-456-2255

Infusion Site Enrollment Form

Please fax this form to:
Biogen Idec
Fax: 1-800-840-1278

The TOUCH Prescribing Program was developed as part of the Biogen Idec 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 compu lsory training conducted by Biogen Idec and faxed a completed Enrollment Form to Biogen Idec. Upon receipt of this Enrollment Form,Bi ogen Idec will fax and mail an authorization confirmation letter to provide your Site Authorization Number and confirm your Shipping Addr ess.

Infusion Site Address (address where patient is infused)

Name of Infusion Site

Contact name

Address 1

Telephone ☐☐☐-☐☐☐-☐☐☐☐

Address 2

Fax ☐☐☐-☐☐☐-☐☐☐☐

City State ZIP

Method of acquiring TYSABRI

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

OR

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. Retal pharmacies and wholesalers are excluded from holding inventory and dispensing TYSABRI.

Shipping Address (address to which drug will be shipped)

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

Name of Infusion Site or Certified Pharmacy

Contact name

Address 1

Telephone ☐☐☐-☐☐☐-☐☐☐☐

Address 2

Fax ☐☐☐-☐☐☐-☐☐☐☐

City State ZIP

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 D iscontinuation 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 Idec within 1 business day of the patient visit regardless of whether or not the patient received the infus ion by:
  - For paper-based infusion sites: sending a copy of the completed Pre-infusion Patient Checklist to Biogen Idec. 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 Idec and/or a third party designated by Biogen Idec
- I understand that noncompliance with the requirements of the TOUCHPrescribing Program will result in de-enrollment of the infus ion site and termination of the authorization to infuse TYSABRI

Responsible party acknowledgment: _____ Date: _____

Name: _____ Title: _____

Please see full Prescribing Information, including Boxed Warning, at www.TYSABRI.com

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TYSABRI (natalizumab)

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mm/yy

3-7237-xx

TouchH PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health
Phone: 1-800-456-2255

TYSABRI
Pre-infusion Patient Checklist

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

Patient name: _____ ___ _____ **Patient Enrollment Number:** _____
First MI Last (Issued by Biogen Idec. Call 1-800-456-2255 or log on to **www.touchprogram.com** f number is not on file.)

Site name: _____ **Site Authorization Number:** _____

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 Idec (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)

Is the patient currently authorized to receive TYSABRI; Yes ☐ No ☐

Yes Continue to next question.

No **STOP—DO NOT INFUSE**. If authorization cannot be verified on-line at www.touchprogram.com **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 Continue to next question. Yes ☐ No ☐

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

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

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

Crohn's disease ONLY

3. In the past month have you taken, or are Yes ☐ No ☐

MS ONLY

3. In the past month, have you taken medicines to Yes ☐ No ☐

STEP 4: Record infusion information.

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

- After discussing the patient s answers, did the prescriber authorize the patient to be infused? Yes ☐ No ☐
- Check here if you were unable to contact the prescriber. (See next page for further instructions.) ☐

Date infused (MM/DD/YYYY): / / **Not infused** ☐

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

Name and signature of staff completing checklist: Date

STEP 5: Submit the Pre-infusion Patient Checklist to Biogen Idec on-line at www.touchprogram.com OR fax to 1-800-840-1278.

TouchH PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health
Phone: 1-800-456-2255

TYSABRI
Pre-infusion Patient Checklist

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

Examples of Immunosuppressants, Antineoplastics, and Immunomodulators

Multiple Sclerosis

Approved MS Therapies:
D methy umerate (EC DERA®)
G at ramer acetate (Copaxone®)
nterferon beta 1a (Reb f® AVONEx®)
nterferon beta 1b (Betaseron®, Extav a®)
ngo mod (G enya™)
M toxantrone (Novantrone®)
Peg nterferon beta 1a (PLEGR DY™)
A emtuzumab (LEM RADA™)
er f unom de (Aubag o®)

Immunosuppressants/Antineoplastics:
Azath opr ne (muran® Azasan®)
C adr b ne (Leustat n®)
Cyc ophospham de (Cytoxan® Neosar®)
Cyc ospor ne (Sand mmune®, Neora ®)
udarab ne phosphate (udara®)
Lef unom de (Arava®)
Mercaptopur ne (Pur netho ®)
Methotrexate (Methotrex® Rheumatrex® rexa ®)
Mycopheno ate mofet (Ce Cept®)
Pemetrexed (A mta®)

Additional Immunomodulators and Immunosuppressants:
Other nterferons (Act mmune® nfergen®, ntron® A
Pegasys® PEG ntron® Rebetron® Roferon® A)
Ada mumab (um ra®)
A efacept (Amev ve®)
A emtuzumab (Campath®)
Anak nra (K neret®)
Dac zumab (Zenapax®)
Efa zumab (Rapt va®)
Etanercept (Enbre ®)
nf x mab (Rem cade®)
ntravenous mmunog obu n (V G)
R tux mab (R tuxan®)
rastuzumab (ercept n®)

Crohn's Disease

Approved TNF-α inhibitors for Crohn's disease:
Inf x mab (Rem cade®)
Ada mumab (Hum ra®)

Immunosuppressants/Antineoplastics:
Approved TNF-α nh b tors
Azath opr ne (Imuran®, Azasan®)
Ch orambuc (Leukeran®)
C adr b ne (Leustat n®)
Cyc ophospham de (Cytoxan®, Neosar®)
Cyc ospor ne (Sand mmune®, Neora ®)
F udarab ne phosphate (F udara®)
Lef unom de (Arava®)
Mercaptopur ne (Pur netho ®)
Methotrexate (Methotrex®, Rheumatrex®, Trexa ®)
Mycopheno ate mofet (Ce Cept®)
Pemetrexed (A mta®)
Th oguan ne (Tab o d®)

Additional Immunomodulators and Immunosuppressants:
Interferon beta-1a (Reb f®, AVONEx®)
Interferon beta-1b (Betaseron®)
A efacept (Amev ve®)
Abatacept (Orenc a®)
Anak nra (K neret®)
Dac zumab (Zenapax®)
Efa zumab (Rapt va®)
Etanercept (Enbre ®)
G at ramer acetate (Copaxone®)
Intravenous mmunog obu n (IVIG)
M toxantrone (Novantrone®)
Other nterferons (Act mmune®, Infergen®, Intron® A, Pegasys®, PEG-Intron®, Rebetron®, Roferon®-A)
R tux mab (R tuxan®)
Trastuzumab (Hercept n®)
Vedo zumab (Entyv o M)

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:

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

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

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

Please see accompanying full Prescribing Information, including Boxed Warning, for important safety information.

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TYSABRI® (natalizumab)

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TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Certified Pharmacy* Enrollment Form

Please fax this form to:
Biogen Idec
Fax: 1-800-840-1278
Phone: 1-800-456-2255

The TOUCH Prescribing Program was developed as part of the Biogen Idec 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 Idec and faxed a completed Enrollment Form to Biogen Idec. Upon receipt of this Enrollment Form, Biogen Idec will fax and mail an Authorization Confirmation Letter to provide your Pharmacy Authorization Number and confirm your Shipping Address. This letter will also provide you with the Site Authorization Numbers of any of your associated infusion sites that have been authorized to infuse TYSABRI.

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

Certified Pharmacy Shipping Address

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

Name of Certified Pharmacy _____

Address 1 _____

Address 2 _____

City _____ State _____ ZIP _____

Contact name _____

NCPDP _____

Title/position _____

Telephone ☐☐☐-☐☐☐-☐☐☐☐

Fax ☐☐☐-☐☐☐-☐☐☐☐

Associated 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 associated infusion sites that have been authorized according to the TOUCH Prescribing Program.

Certified Pharmacy Acknowledgment

The pharmacy has received training and educational materials on the TOUCH Prescribing Program for use in the following indication(s): MS ☐ CD ☐ (check all that apply)

Certified pharmacies may dispense TYSABRI only to authorized infusion sites

- I understand that, per the requirements of the TOUCH Prescribing Program, this certified pharmacy's compliance may be reviewed by the Food and Drug Administration (FDA), and/or audited by Biogen Idec, and/or a third party designated by Biogen Idec.
- 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 accompanying full Prescribing Information.

biogen idec®

TYSABRI® (natalizumab)

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Reference ID: 3753128

TouchH® PRESCRIBING PROGRAM

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Please see full Prescribing Information, including Boxed Warning, for important safety information.

TYSABRI® (natalizumab)

Reference ID: 3753128

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

TOUCH® PRESCRIBING PROGRAM
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Indications and Usage – Multiple Sclerosis

- TYSABRI® (natalizumab) is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis.
- TYSABRI increases the risk of PML.
- When initiating and continuing treatment with TYSABRI, physicians should consider whether the expected benefit of TYSABRI is sufficient to offset this risk.
- See Full Prescribing Information regarding the risk of PML with TYSABRI.

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Indications and Usage – Crohn's Disease

- TYSABRI® is indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-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 progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability.
- Risk factors for the development of PML include duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. 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®, and for six months following discontinuation of 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.

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.

Reference ID: 3753128

Warnings and Precautions - PML

- Three factors that are known to increase the risk of PML in TYSABRI-treated patients have been identified:
  - Longer treatment duration, especially beyond 2 years. There is limited experience in patients who have received more than 6 years of TYSABRI treatment
  - Prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil)
  - The presence of anti-JCV antibodies. Patients who are anti-JCV antibody positive have a higher risk for developing PML
- These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI.

Warnings and Precautions – PML

- Infection by the JC virus 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 exposure to the JC virus has 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

- 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.
- Anti-JCV antibody testing should not be performed for at least two weeks following plasma exchange due to the removal of antibodies from the serum.

Warnings and Precautions – 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, TYSBARI should be discontinued, and appropriate treatment for herpes encephalitis/meningitis should be administered.

Warnings and Precautions – Hepatotoxicity

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

Warnings and Precautions – Hypersensitivity/Antibody Formation

- TYSABRI has been associated with hypersensitivity reactions, including serious systemic reactions (e.g., anaphylaxis), which occurred at an incidence of <1%.
- Patients who receive TYSABRI after an extended period without treatment may be at higher risk of hypersensitivity reactions.
- If a hypersensitivity reaction occurs, discontinue the use of TYSABRI, and initiate appropriate therapy.
- Do not re-treat with TYSABRI.

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.

Adverse Reactions

- The most frequently reported serious adverse reactions in the Study MS1 were infections (3.2% vs 2.6% placebo), acute hypersensitivity reactions (1.1% vs 0.3%), depression (1.0% vs 1.0%), and cholelithiasis (1.0% vs 0.3%).

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

Adverse Reactions (cont'd)

- The most common adverse reactions reported at an incidence of >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.

TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

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® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

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

Reference ID: 3753128

What was 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 longer treatment duration, prior immunosuppressant use, and the presence of anti-JCV antibodies
- 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

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What are the program requirements?

Prescribers

Infusion Sites

Pharmacies

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

Prescribe TYSABRI®

Infuse TYSABRI

Dispense TYSABRI

Patients

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

Receive TYSABRI

TOUCH® PRESCRIBING PROGRAM
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TOUCH Prescribing Program Components

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.

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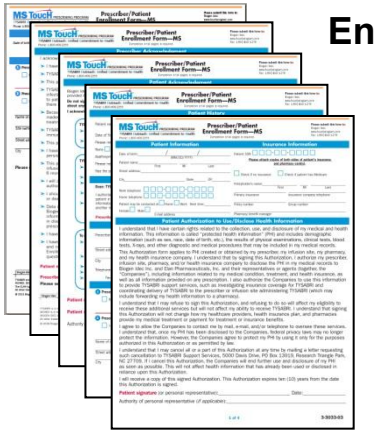
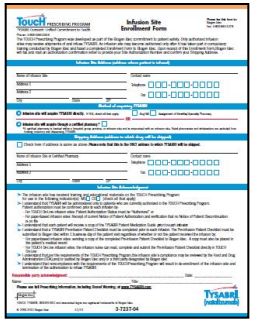
Tools to Support the TOUCH Prescribing Program – MS

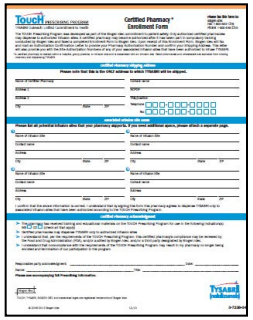
Enrollment Forms



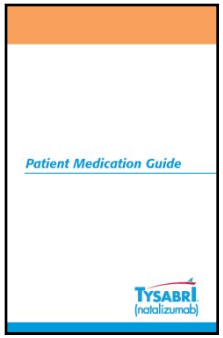
Prescriber/Patient



Infusion Site

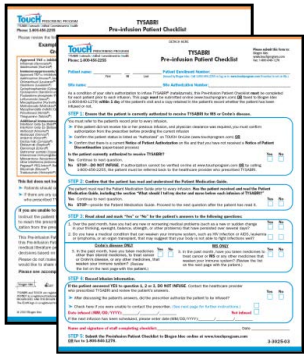


Certified Pharmacy

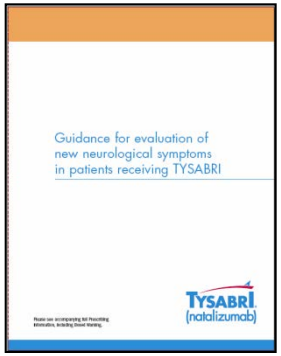


Patient Medication Guide

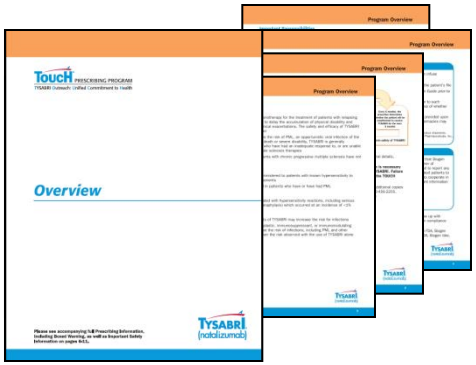
Notice of Patient Authorization



Pre-infusion Patient Checklist



Guidance for Evaluation of New Neurological Symptoms in Patients Receiving TYSABRI®



TOUCH Prescribing Program Overview

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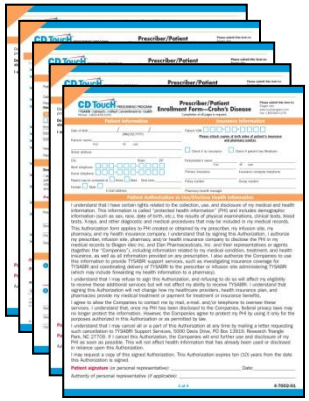
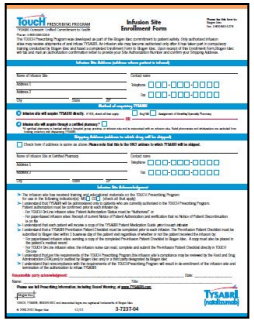
Tools to Support the TOUCH Prescribing Program – Crohn's Disease

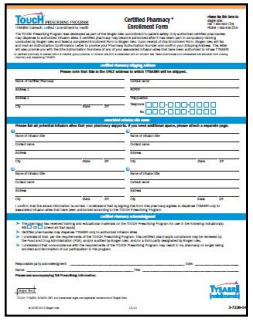
Enrollment Forms



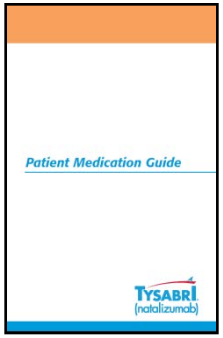
Prescriber/Patient



Infusion Site

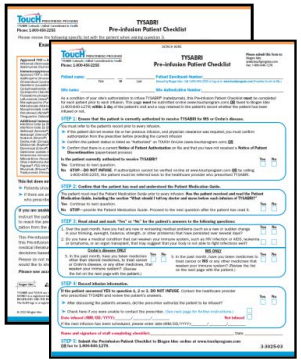


Certified Pharmacy

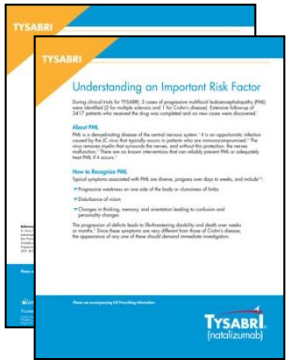


Patient Medication Guide

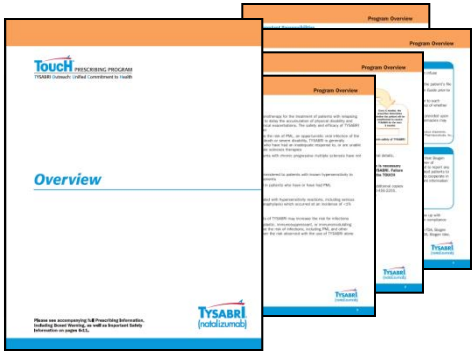
Notice of Patient Authorization



Pre-infusion Patient Checklist



Understanding PML for Gastroenetrologists



TOUCH Prescribing Program Overview

TOUCH PRESCRIBING PROGRAM
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How Do I Communicate With TOUCH?

WEB

PHONE

1-800-456-2255

Monday – Friday 8:30AM – 8PM EST

PAPER

Fax: 1-800-840-1278

TouchH PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

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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 Idec and/or a third party designated by Biogen Idec
- 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

TOUCH® PRESCRIBING PROGRAM
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TOUCH® PRESCRIBING PROGRAM
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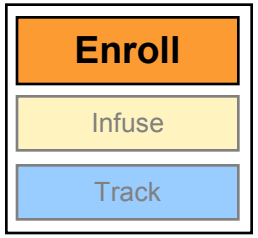
Prescriber/Patient Enrollment



TouchH® PRESCRIBING PROGRAM
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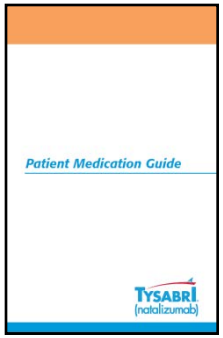
How do prescribers and patients enroll?

Enroll
Infuse
Track

Education

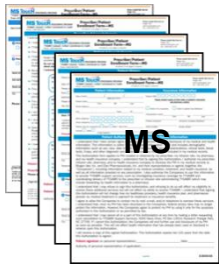
Prescriber and Patient discuss TYSABRI® as a treatment option

Treatment Decision

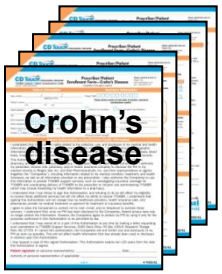


Patient reads the **Patient Medication Guide** and discusses the benefits and risks of TYSABRI with his/her prescriber.

Enrollment

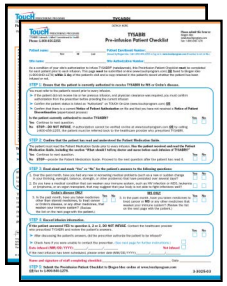


or



Prescriber and patient complete, sign, and fax ALL PAGES of the **Prescriber/Patient Enrollment Form** to the TOUCH Prescribing Program to initiate therapy.

Prescriber reviews **Pre-infusion Patient Checklist** with the patient.



Authorization

TOUCH Case Manager confirms that all paperwork is complete and updates patient status to **'Authorized'**

TOUCH On-Line
www.touchprogram.com

OR

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

TOUCH® PRESCRIBING PROGRAM
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MS TouchH® PRESCRIBING PROGRAM
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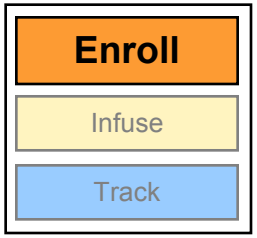
Enrollment Tools



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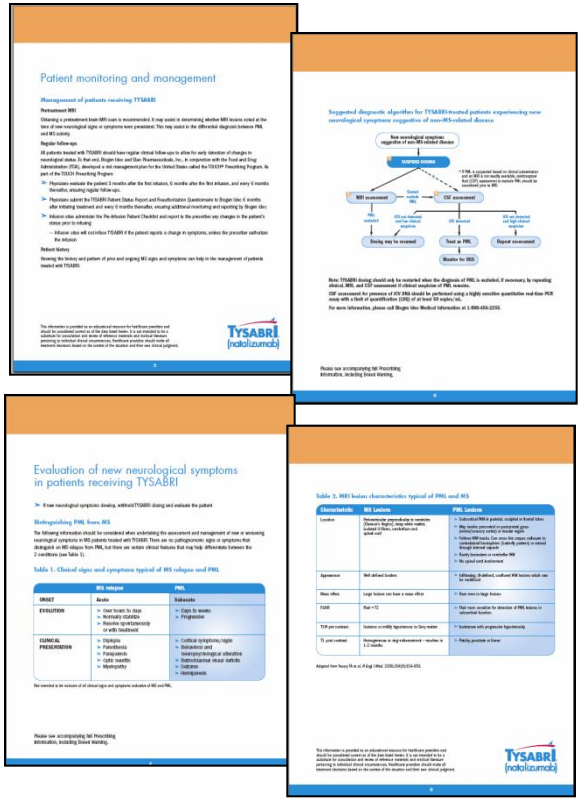
Guidance for Evaluation of New Neurological Symptoms in Patients Receiving TYSABRI®

Brochure provided by Biogen Idec

Resource for: Neurology specialists



Key topics include:

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

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

TouchPRESCRIBING PROGRAM
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CD TouchH® PRESCRIBING PROGRAM
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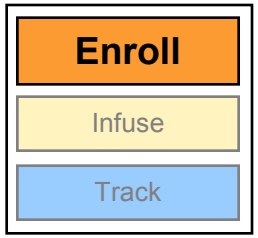
Enrollment Tools



Understanding PML

Flashcard provided by Biogen Idec

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

TYSABRI

Action Steps if PML Is Suspected

TYSABRI

Understanding an Important Risk Factor

About PML

How to Recognize PML

TYSABRI (natalizumab)

Key topics include:

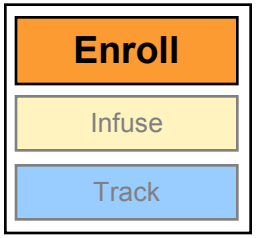
- Characteristics of PML
- Guidance on recognizing PML in context of Crohn's disease
- Action steps if PML is suspected

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.

TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

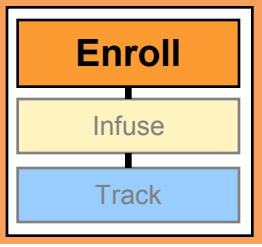
Reference ID: 3753128

Infusion Site Enrollment

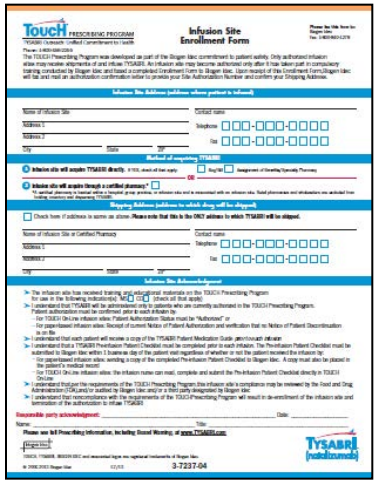


TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

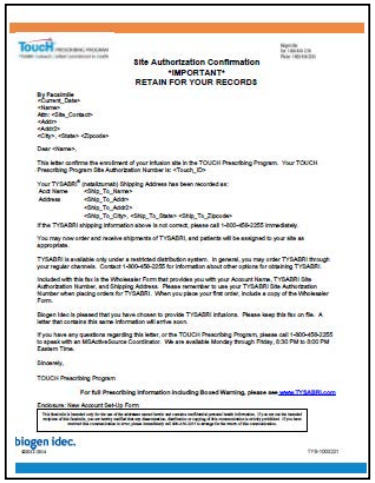
How does an Infusion Site enroll?



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



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



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

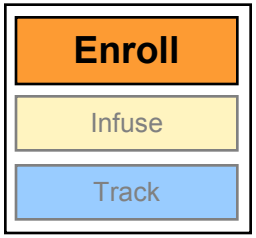
* NOTE: Infusion Sites must select to receive training and education materials on MS TOUCH, CD TOUCH, or both.

A patient will be matched **ONLY** with Infusion Sites that have been trained on the program materials related to his/her indication.

TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

Certified Pharmacy Enrollment

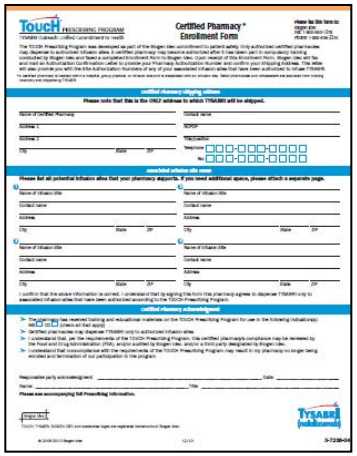


TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

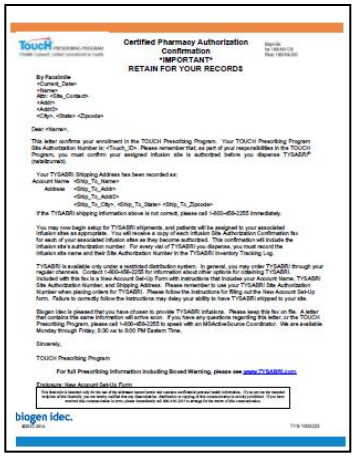
Reference ID: 3753128

How does a Certified Pharmacy* enroll?

A Biogen Idec representative provides training to the **Certified Pharmacy** regarding the TOUCH Prescribing Program



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



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

*A Certified Pharmacy is located within a hospital, group practice, or infusion site and is associated with an infusion site.

TouchPRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

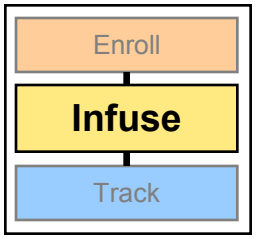
Program Overview

- 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® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

Infusion Overview



TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

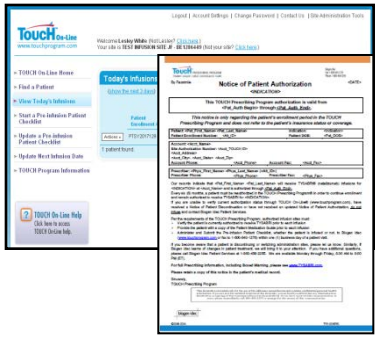
What process must be completed in order to infuse TYSABRI®?

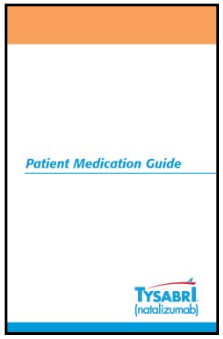
Enroll
Infuse
Track

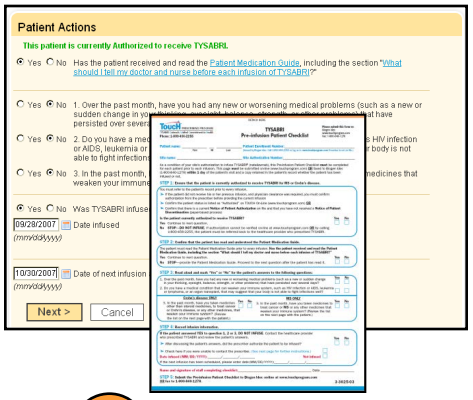
TYSABRI should NOT be prepared until the **Pre-infusion Patient Checklist** has been successfully completed

Patient arrives for TYSABRI infusion

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*

Infusion

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

- Start an IV line
- Mix TYSABRI

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

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

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

TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

Checking Patient Authorization Status

Enroll
Infuse
Track

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

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

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

TOUCH PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Biogen Idec
Fax: 1-800-848-1238
Phone: 1-800-456-2255

Notice of Patient Authorization

<DATE>

<INDICATION>

This TOUCH Prescribing Program authorization is valid from 10/12/2007 through 4/11/2008.

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

Patient: Jennifer Patient
Patient Enrollment Number: XXXXXXXXXX
Indication: <indication>
Patient DOB: 01/01/1978

Account: Infusion Site
Site Authorization Number: BE1290291
111 Infusion Lane
Las Vegas, NV 89118
Account Phone: 555-555-5558
Account Fax: 555-555-5559

Prescriber: TYSABRI Physician MD123456789
Prescriber Phone: 555-555-5555
Prescriber Fax: 555-555-5556

Today's Infusions

(show the next 3 days)

Patient Enrollment #	Last Name	First Name	Date of Birth	Status	Last Infusion Date	Next Infusion Date	Pre-Infusion Patient Checklist Status
	PATIENT	JENNIFER	01/01/1978	Authorized	10/12/2007	09/28/2007	Start

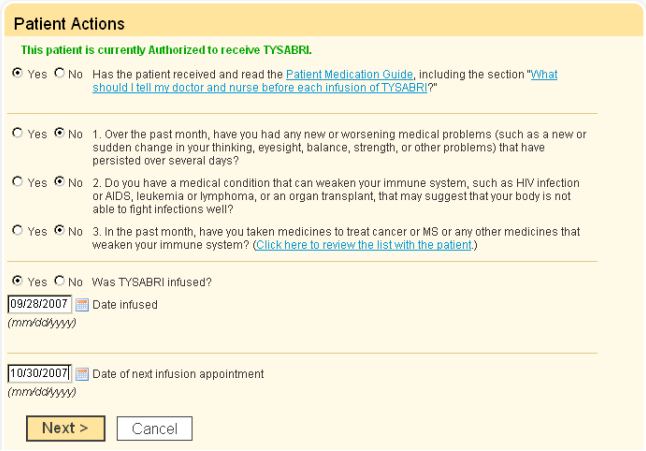
1 patient found.

TOUCH PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

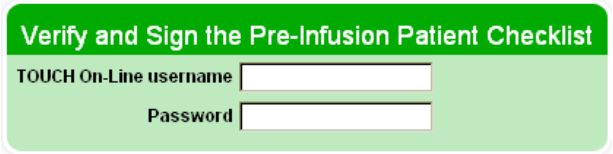
Reference ID: 3753128

Pre-infusion Patient Checklist

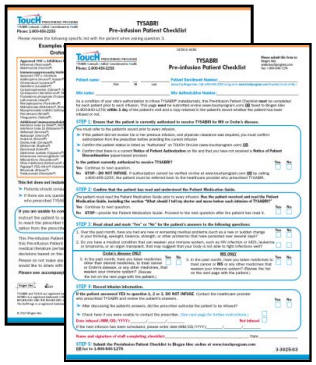
- All Infusion Sites must complete, sign, and submit the **Pre-infusion Patient Checklist** at <u>every</u> infusion visit



- 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 **<u>must</u>** be completed and submitted whether or not the patient is infused.

TOUCH PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

Program Overview

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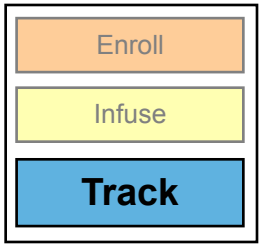
- What is the process to infuse TYSABRI®?
- **How are patients tracked?**
- What is TOUCH On-Line?

TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

Tracking Overview



TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

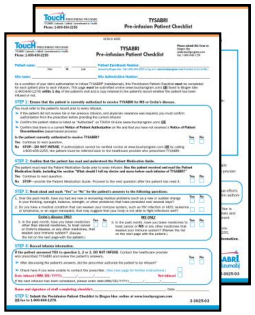
Tracking Overview

Enroll
Infuse
Track

Infusion Site

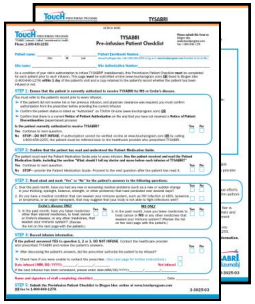
Pre-infusion Patient Checklist

MS



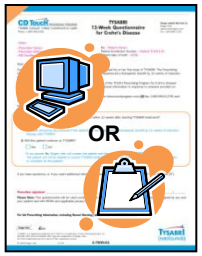
OR

Crohn's disease



Prescriber

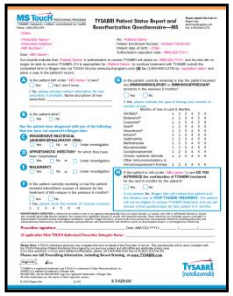
12-Week Questionnaire



OR

Prescriber

Patient Status Report and Reauthorization Questionnaire



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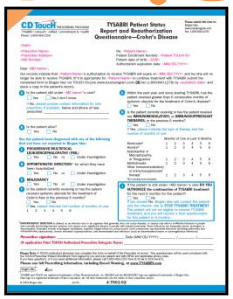
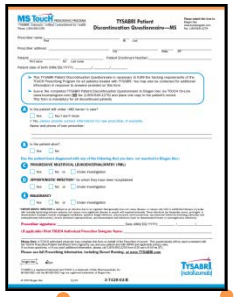


Prescriber

Initial and 6-Month Discontinuation Questionnaire



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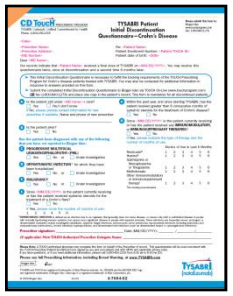


NOTE: Missing or incomplete TOUCH Prescribing Program forms will prompt continued follow-up by a TOUCH Compliance Manager.

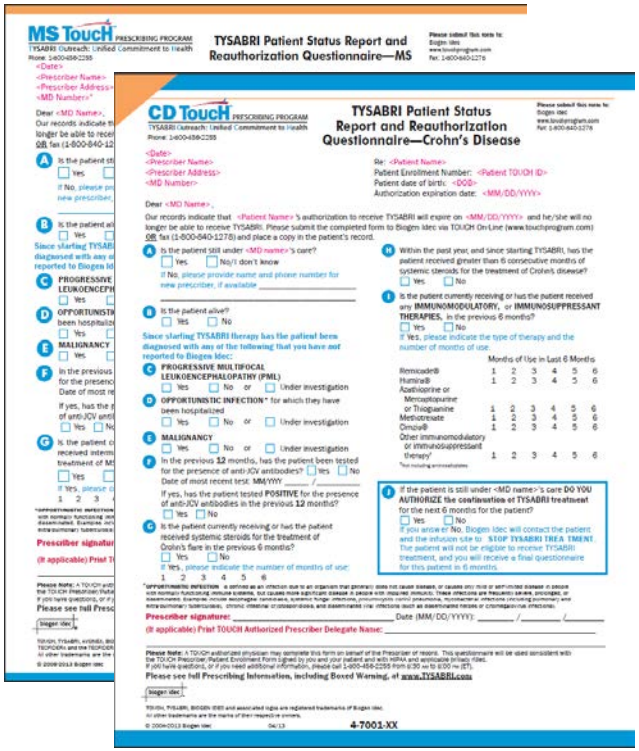
TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

Prescriber Must Reauthorize the Use of TYSABRI® Every 6 Months

Enroll
Infuse
Track

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

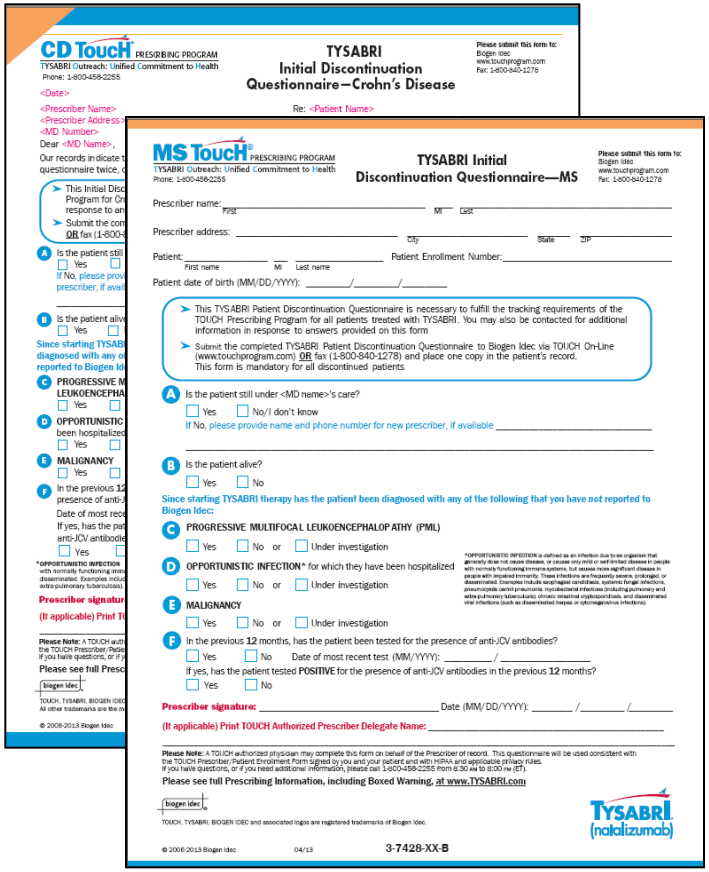
OR

TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

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

Enroll
Infuse
Track


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

TYSABRI
Initial Discontinuation
Questionnaire—Crohn's Disease

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

Re: <Patient Name>

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

TYSABRI Initial
Discontinuation Questionnaire—MS

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

Prescriber name: _____ First _____ MI _____ Last _____

Prescriber address: _____ City _____ State _____ ZIP _____

Patient: _____ First name _____ MI _____ Last name _____ Patient Enrollment Number: _____

Patient date of birth (MM/DD/YYYY): _____/_____/_____

- This TYSABRI Patient Discontinuation Questionnaire is necessary to fulfill the tracking requirements of the TOUCH Prescribing Program for all patients treated with TYSABRI. You may also be contacted for additional information in response to answers provided on this form
- Submit the completed TYSABRI Patient Discontinuation Questionnaire to Biogen Idec 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 Idec:

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 In the previous **12** months, has the patient been tested for the presence of anti-JCV antibodies?
☐ Yes ☐ No Date of most recent test (MM/YYYY): _____ / _____
If yes, has the patient tested **POSITIVE** for the presence of anti-JCV antibodies in the previous **12** months?
☐ Yes ☐ No

*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).

Prescriber signature: _____ Date (MM/DD/YYYY): _____ /_____/_____

(If applicable) Print TOUCH Authorized Prescriber Delegate Name: _____

Please Note: A TOUCH authorized physician may complete this form on behalf of the Prescriber of record. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient and with HIPAA and applicable privacy rules.
If you have questions, or if you need additional information, please call 1-800-456-2255 from 6:30 AM to 8:00 PM (ET).

Please see full Prescribing Information, including Boxed Warning, at www.TYSABRI.com

biogen idec

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TYSABRI (natalizumab)

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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

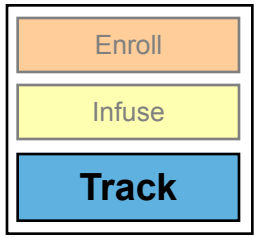
***NOTE: Discontinuation Questionnaires are ONLY sent upon notification of discontinuation and again six months following discontinuation of TYSABRI**

TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

MS TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Tracking Tools

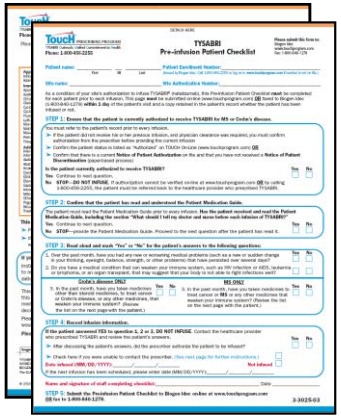


TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

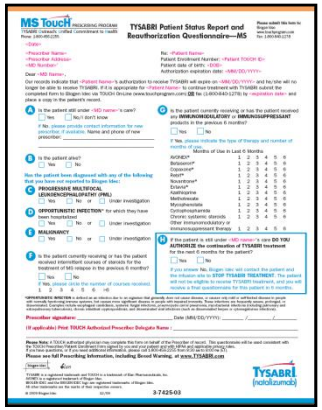
Tracking Overview – MS

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

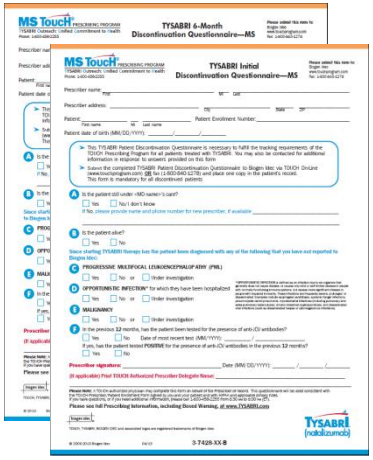
Pre-infusion Patient Checklist (Every 28 days)



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



Initial and 6-Month Discontinuation Questionnaire*



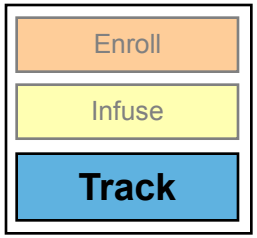
***NOTE: Discontinuation Questionnaires are ONLY sent upon notification of discontinuation and again six months following discontinuation of TYSABRI**

TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

CD TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Tracking Tools

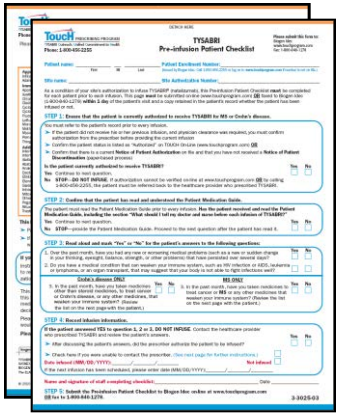


TouchH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

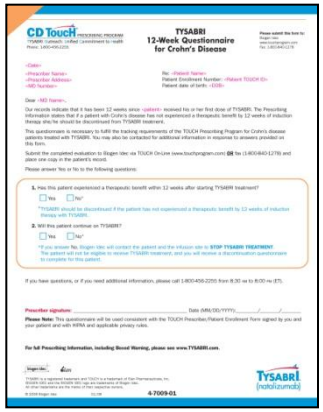
Tracking Overview – Crohn's Disease

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

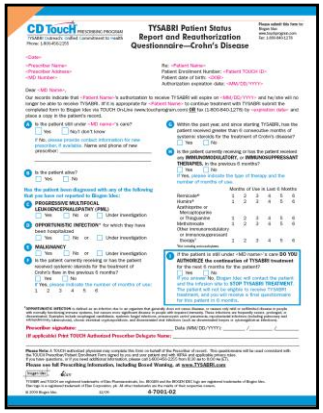
Pre-infusion Patient Checklist (Every 28 days)



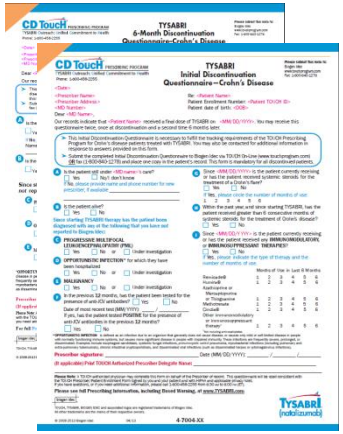
12-Week Questionnaire (After initial 12 weeks)



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.**

TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

Program Overview

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

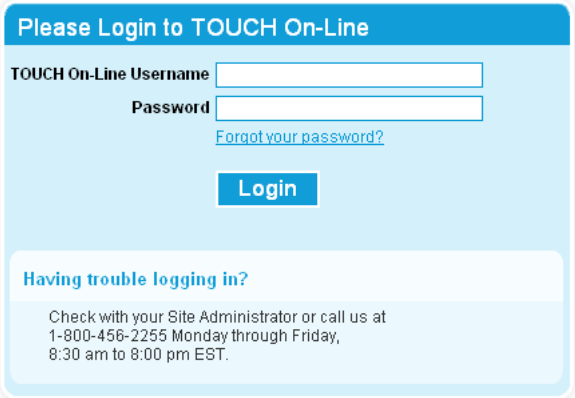
TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

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

TOUCH® On-Line
www.touchprogram.com

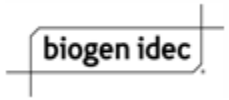


TOUCH® PRESCRIBING PROGRAM
TYSABRI Outreach: Unified Commitment to Health

Reference ID: 3753128

Summary Review

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



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Reference ID: 3753128

TouchH® PRESCRIBING PROGRAM

TYSABRI Outreach: Unified Commitment to Health

Overview

Please see accompanying full Prescribing Information, including Boxed Warning, as well as Important Safety Information on pages 6-9.

TYSABRI® (natalizumab)

INDICATIONS AND USAGE

Multiple Sclerosis (MS)

- TYSABRI (natalizumab) is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. TYSABRI increases the risk of PML. When initiating and continuing treat ment with TYSABRI, physicians should consider whether the expected benefit of TYSABRI is suffi cient to offset this risk. See Full Prescribing Information regarding the risk of PML with TYSABRI

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 mercap topurine, azathioprine, cyclosporine or methotrexate) or inhibitors of TNF α

Why the program was developed

Biogen Idec 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 longer treatment duration, prior immunosuppressant use, and the presence of anti JCV antibodies
- 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 associated with infusion sites, 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 Idec at 1 800 840 1278.

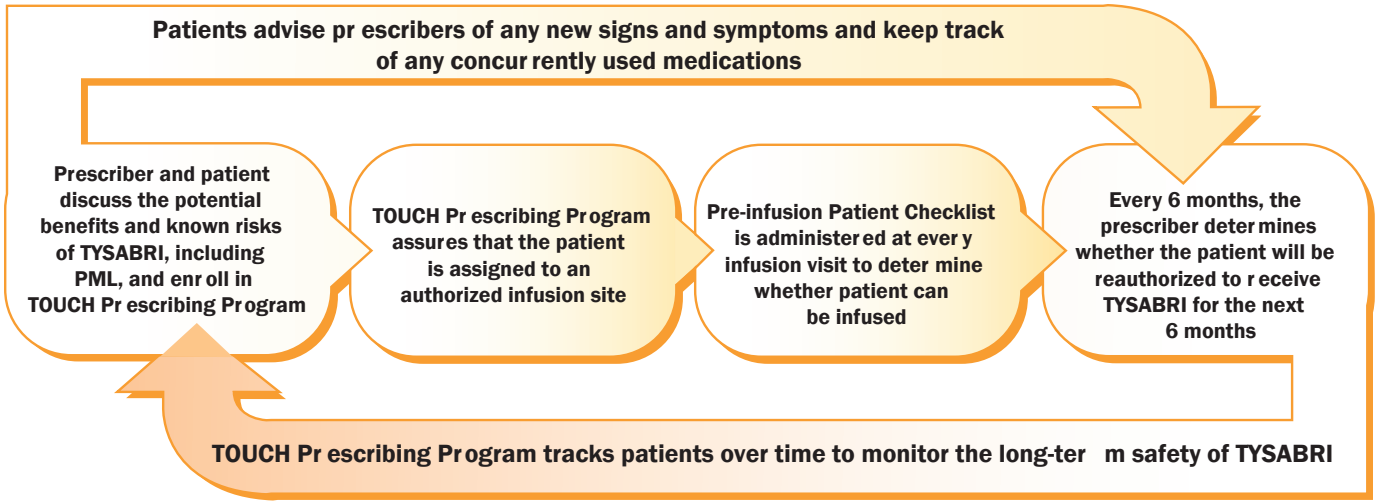
Please see accompanying full Prescribing Information, including Boxed Warning, as well as Important Safety Information on pages 6-9.

Reference ID: 3753128

TOUCH On-Line
www.touchprogram.com

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

How the program works



This Overview serves only as an introduction to the program. For additional details please see the full 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 Idec representative or call 1 800 456 2255, 8:30 AM to 8:00 PM (ET). The Patient Medication Guide is also available online at **www.TYSABRI.com**.

TYSABRI (natalizumab)

1 Enrollment

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

Prescribers and Patients
Prior to enrollment, prescribers must receive and review the full 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 Idec 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 associated certified pharmacies must receive training from a Biogen Idec 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 accompanying full Prescribing Information, including Boxed Warning, as well as Important Safety Information on pages 6-9.

Reference ID: 3753128

2 Infusion

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

- Confirm that the patient is currently authorized to receive TYSABRI
- Provide the patient with a copy of the TYSABRI Patient Medication Guide prior to each infusion
- Administer the Pre Infusion Patient Checklist to every patient prior to each infusion and submit it to Biogen Idec 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, associated 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 Idec and authorized certified pharmacies associated with authorized infusion sites.

3 Tracking

The TOUCH Prescribing Program will track all patients over time so that Biogen Idec 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 Idec 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 Idec, and/or a third party authorized by Biogen Idec.

TYSABRI® (natalizumab)

IMPORTANT SAFETY INFORMATION

Indication

TYSABRI (natalizumab) is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. TYSABRI increases the risk of PML. When initiating and continuing treatment with TYSABRI, physicians should consider whether the expected benefit of TYSABRI is sufficient to offset this risk. See important information regarding the risk of PML with TYSABRI.

WARNING

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 duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. 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.

Progressive Multifocal Leukoencephalopathy (PML)

- Infection by the JC Virus is required for the development of PML.
- Anti JCV antibody testing should not be used to diagnose PML.
- 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.
- PML has been reported following 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 six months following dis continuation of TYSABRI.
- In MS patients, an MRI scan should be obtained prior to initiating therapy with TYSABRI. This MRI may be helpful in differentiating subsequent multiple sclerosis symptoms from PML.
- Three sessions of plasma exchange 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 which may occur during plasma exchange include clearance of other medications and volume shifts, which have the potential to lead to hypotension or pulmonary edema. Although plasma exchange has not been 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.
- Anti JCV antibody testing should not be performed during or for at least two weeks following plasma exchange due to the removal of antibodies from the serum.

Please see accompanying full Prescribing Information, including Boxed Warning.

TYSABRI (natalizumab)

Reference ID: 3753128

- 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 neu rological 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.

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.
- FFor 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 dis ease).
- Prescribers must be certified and comply with the following:

  Review the TOUCH Prescribing Program prescriber educational materials, including the full 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 Idec 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 Idec 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.

TYSABRI (natalizumab)

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, TYSBARI should be discontinued, and appropriate treatment for herpes encephalitis/meningitis should be administered.

Hepatotoxicity

- Clinically significant liver injury, including acute liver failure requiring transplant, has been reported in patients treated with TYSABRI in the postmarketing setting. In some patients, liver injury recurred upon rechallenge, providing evidence that TYSABRI caused the injury.
- 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 obstruc tion 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 sys temic 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 antibod ies to TYSABRI.
- If a hypersensitivity reaction occurs, discontinue administration of TYSABRI, and initiate appro priate 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 after an extended period without treatment may be at higher risk of hypersensitivity reactions.

Immunosuppression/Infections

- The immune system effects of TYSABRI may increase the risk for infections.

Please see accompanying full Prescribing Information, including Boxed Warning.

TYSABRI (natalizumab)

- In Study MS1, certain types of infections, including pneumonias and urinary tract infections (including serious cases), gastroenteritis, vaginal infections, tooth infections, tonsillitis, and her pes 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 receiv ing 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 Study MS1 and Study 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 per sisted 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 that are frequently transient.

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% versus 0.3%) and pneumonia (0.6% versus 0%), acute hypersensitivity reactions (1.1% vs 0.3%, including anaphylaxis/anaphylac toid reaction [0.8% versus 0%]), depression (1.0% vs 1.0%, including suicidal ideation or attempt [0.6% versus 0.3%]), and cholelithiasis (1.0% vs 0.3%).
- Based on animal data, TYSABRI may cause fetal harm. TYSABRI should be used during preg nancy only if the potential benefit justifies the potential risk to the fetus.

Please see accompanying full Prescribing Information, including Boxed Warning.

TYSABRI® (natalizumab)

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 Idec 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 Idec 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 *eac*
- Administer the Pre infusion Patient Checklist to every patient prior to each infusion and submit to Biogen Idec within 1 business day, regardless of whether the patient is infused or not

Please see accompanying full Prescribing Information, including Boxed Warning, as well as Important Safety Information on pages 6-9.

biogen idec®

TYSABRI® (natalizumab)

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Reference ID: 3753128

SUPPORT TOUCH® On-Line
www.touchprogram.com

- TOUCH On-Line Login
- How do I enroll in the TOUCH Prescribing Program?
- TOUCH Prescribing Program Resources
- Learn more about TYSABRI
- Prescribing Information
- Patient Medication Guide
- Patient Medication Guide - Spanish

Not a TOUCH On-Line user?

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

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

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

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

The TOUCH Prescribing Program is designed to:

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

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

TOUCH On-Line Login

TOUCH On-Line Username

Password

Please note that the password is case sensitive.

My password is not working, please e-mail me my password - click here

Login

Having trouble logging in?

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

Indications

Multiple Sclerosis (MS)
TYSABRI (natalizumab) is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. TYSABRI increases the risk of PML. When initiating and continuing treatment with TYSABRI, physicians should consider whether the expected benefit of TYSABRI is sufficient to offset this risk. See important information regarding the risk of PML with TYSABRI.

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 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.

WARNING
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 duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. 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. At the first sign or symptom that may be suggestive of PML, TYSABRI dosing should be withheld immediately. 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.

Progressive Multifocal Leukoencephalopathy (PML)

- Infection by the JC Virus is required for the development of PML.
- Anti-JCV antibody testing should not be used to diagnose PML.
- 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.
- PML has been reported following 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 six months after discontinuation of TYSABRI.
- In MS patients, an MRI scan should be obtained prior to initiating therapy with TYSABRI. This MRI may be helpful in differentiating subsequent multiple sclerosis symptoms from PML.
- Three sessions of plasma exchange over the course of 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 which may occur during plasma exchange include clearance of other medications and volume shifts, which have the potential to lead to hypotension or pulmonary edema. Although plasma exchange has not been 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.
- Anti-JCV antibody testing should not be performed during or for at least two weeks following plasma exchange due to the removal of antibodies from the serum.
- 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.

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 full 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 Idec 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 Idec 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.

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.
- 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.

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 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).

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 to patients who did not develop antibodies to TYSABRI in both MS and CD studies.
- Patients who receive TYSABRI after an extended period without treatment may be at higher risk of hypersensitivity reactions.

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 that are frequently transient.

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% versus 0.3%) and pneumonia (0.6% versus 0%), acute hypersensitivity reactions (1.1% vs 0.3%, including anaphylaxis/anaphylactoid reaction [0.8% versus 0%]), depression (1.0% vs 1.0%, including suicidal ideation or attempt [0.6% versus 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.

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- TOUCH On-Line Login
- How do I enroll in the TOUCH Prescribing Program?
- TOUCH Prescribing Program Resources
- Learn more about TYSABRI
- Prescribing Information
- Patient Medication Guide
- Patient Medication Guide - Spanish

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 Idec.
  - 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 Idec 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 Idec 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 Idec 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 Idec, call toll free: 1-800-456-2255 Monday-Friday, 8:30 AM to 8:00 PM (ET).

Indications

Multiple Sclerosis (MS)
TYSABRI (natalizumab) is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. TYSABRI increases the risk of PML. When initiating and continuing treatment with TYSABRI, physicians should consider whether the expected benefit of TYSABRI is sufficient to offset this risk. See important information regarding the risk of PML with TYSABRI.

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 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.

WARNING
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 duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. 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. At the first sign or symptom that may be suggestive of PML, TYSABRI dosing should be withheld immediately. 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.

Progressive Multifocal Leukoencephalopathy (PML)

- Infection by the JC Virus is required for the development of PML.
- Anti-JCV antibody testing should not be used to diagnose PML.
- 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.
- PML has been reported following 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 six months after discontinuation of TYSABRI.
- In MS patients, an MRI scan should be obtained prior to initiating therapy with TYSABRI. This MRI may be helpful in differentiating subsequent multiple sclerosis symptoms from PML.
- Three sessions of plasma exchange over the course of 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 which may occur during plasma exchange include clearance of other medications and volume shifts, which have the potential to lead to hypotension or pulmonary edema. Although plasma exchange has not been 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.
- Anti-JCV antibody testing should not be performed during or for at least two weeks following plasma exchange due to the removal of antibodies from the serum.
- 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.

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.
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- Prescribers must be certified and comply with the following:
  - Review the TOUCH Prescribing Program prescriber educational materials, including the full 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 Idec 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 Idec 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.
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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.
- 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.

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 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).

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 to patients who did not develop antibodies to TYSABRI in both MS and CD studies.
- Patients who receive TYSABRI after an extended period without treatment may be at higher risk of hypersensitivity reactions.

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 that are frequently transient.

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% versus 0.3%) and pneumonia (0.6% versus 0%), acute hypersensitivity reactions (1.1% vs 0.3%, including anaphylaxis/anaphylactoid reaction [0.8% versus 0%]), depression (1.0% vs 1.0%, including suicidal ideation or attempt [0.6% versus 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.

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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 Idec 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
- **Diagnosing PML (progressive multifocal leukoencephalopathy)**
  - Guidance 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.
    - Guidance 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 Idec, call toll free: 1-800-456-2255 Monday-Friday, 8:30 AM to 8:00 PM (ET).

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Crohn's Disease (CD)
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WARNING
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Healthcare professionals should monitor patients on TYSABRI for any new sign or symptom that may be suggestive of PML. At the first sign or symptom that may be suggestive of PML, TYSABRI dosing should be withheld immediately. 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.

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Progressive Multifocal Leukoencephalopathy (PML)

- Infection by the JC Virus is required for the development of PML.
- Anti-JCV antibody testing should not be used to diagnose PML.
- 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.
- PML has been reported following 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 six months after discontinuation of TYSABRI.
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- Anti-JCV antibody testing should not be performed during or for at least two weeks following plasma exchange due to the removal of antibodies from the serum.
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Hepatotoxicity

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- 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).

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%.
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- Hypersensitivity reactions were more frequent in patients with antibodies to TYSABRI compared to patients who did not develop antibodies to TYSABRI in both MS and CD studies.
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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 that are frequently transient.

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% versus 0.3%) and pneumonia (0.6% versus 0%), acute hypersensitivity reactions (1.1% vs 0.3%, including anaphylaxis/anaphylactoid reaction [0.8% versus 0%]), depression (1.0% vs 1.0%, including suicidal ideation or attempt [0.6% versus 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.

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