MADISON NEUROLOGY LLC

608 403 0000

Neurology Care 7 days a Week. Because Your Brain Matters.

Tysabri®

Natalizumab

COMPLETE CLINICAL PROTOCOL: PRE-TREATMENT CHECKLIST • ORDER SET • FOLLOW-UP • HOLD/DISCONTINUE CRITERIA

GENERIC NAME	natalizumab
BRAND	TYSABRI®
MEDICATION CLASS	α4-integrin antagonist monoclonal antibody (selective adhesion-molecule inhibitor)
PRESENTATION	300 mg/15 mL (20 mg/mL) single-dose vial — dilute in 100 mL 0.9% sodium chloride
ROUTE	IV infusion over approximately 1 hour, every 4 weeks
US INDICATION (FDA)	Relapsing forms of MS in adults — generally reserved for highly active disease or inadequate response/intolerance to alternatives because of PML risk; also Crohn's disease.

Class context.
Natalizumab does not deplete lymphocytes — its dominant risk is PML from impaired CNS immune surveillance, which drives the entire monitoring architecture (JCV index, MRI cadence, TOUCH).

REMS-restricted program.
Tysabri is available only through the TOUCH® Prescribing Program. Prescriber, patient, infusion site, and pharmacy must all be enrolled; patient authorization is re-confirmed before each dose; prescribers re-enroll periodically and report serious adverse events to the program.

Section 1 — Pre-Treatment Checklist

A. Required screening labs

☐ Anti-JCV antibody with INDEX value — REQUIRED baseline and the pivot of PML risk stratification (negative → ~0.1/1000 risk; positive with prior immunosuppression or >2 years' exposure → up to ~1/100).

- ☐ Baseline brain MRI (with and without gadolinium) — mandatory reference; PML-vs-relapse discrimination at 3 a.m. depends on it.
- ☐ Prior-immunosuppression inventory: mitoxantrone, cyclophosphamide, azathioprine, mycophenolate, methotrexate, or chronic immunosuppression each raise PML risk and must be documented in TOUCH.
- ☐ CBC with differential; baseline LFTs (transaminase elevations and liver injury reported).
- ☐ Pregnancy test for females of reproductive potential.

B. Vaccinations

- ☐ No live-vaccine prohibition in the US label, but complete needed immunizations before starting an immunomodulator per institutional practice; avoid adding live vaccines during treatment without specialist review.

C. Clinical assessments & counseling

- ☐ Neurologic examination with EDSS at baseline and periodically.
- ☐ TOUCH enrollment completed: prescriber certification, patient acknowledgement, infusion-site enrollment, baseline MRI upload per program rules.
- ☐ PML symptom education with a written checklist the patient reviews before EVERY dose (new/worsening weakness, vision, speech, cognition, personality, coordination).
- ☐ Document rationale (highly active disease or inadequate response) — supports both the REMS file and payer authorization.

D. Exclusion / hold criteria — do not start

CRITERION	RATIONALE / REQUIRED ACTION
Known or suspected PML	Absolute labeled contraindication.
Hypersensitivity/anaphylaxis to natalizumab	Labeled contraindication.
Concurrent immunosuppressants/antineoplastics for MS	Contraindicated combination — surveillance impairment compounds.
Active significant infection	Defer until resolved.

Section 2 — Order Set

Premedication

- ☐ None required by label. For prior mild infusion reactions: acetaminophen ± antihistamine per institutional practice.

Dosing schedule

Standard dose	300 mg IV in 100 mL 0.9% NaCl over approximately 1 hour, every 4 weeks.
Observation	Observe during the infusion and for 1 hour after completion for hypersensitivity (urticaria, anaphylaxis typically occur within 2 hours of start).
Extended-interval dosing	Every-6-week schedules are used in practice to reduce PML exposure; this is an off-label risk-mitigation strategy — document the rationale and program requirements.

Standing orders — every infusion

☐ Pre-dose PML symptom checklist and interval-neurology review before EVERY infusion (TOUCH).

☐ Confirm no contraindicated concurrent immunosuppression was started elsewhere.

☐ Vital signs per infusion-center protocol; treat hypersensitivity by severity (interrupt → discontinue if anaphylaxis).

Missed or delayed dose

Resume as soon as feasible; keep the every-4-week cadence. If interruption extends beyond ~8–12 weeks, reassess rebound disease-activity risk and plan transition therapy rather than indefinite gap.

Contraception & pregnancy

Natalizumab crosses the placenta (third-trimester fetal thrombocytopenia/anemia reported). Discuss pregnancy planning; most programs continue through pregnancy only after individualized risk-benefit review.

Section 3 — Follow-Up Protocol

ITEM	FREQUENCY / TIMING	ACTION / THRESHOLD
Anti-JCV antibody with index	Every 6 months while seronegative; seropositives tracked per program	Seroconversion or rising index → re-counsel, re-stratify, reconsider continuation.
Brain MRI	At least annually; every 3–6 months in higher-risk patients (JCV+, index rising, prior IS use, >2 years on drug)	Any PML-suggestive lesion or symptom → hold dosing, urgent PML-protocol MRI ± CSF JCV DNA.
TOUCH compliance	Before every dose	Do not infuse without current authorization.
Anti-natalizumab antibodies	If persistent hypersensitivity or loss of efficacy	Persistently positive antibodies → discontinue (no efficacy, reaction risk).
LFTs	If symptoms/signs of liver injury	Significant injury → discontinue.

Section 4 — Pause vs. Stop Criteria

A. Pause or delay (resume when resolved)

CRITERION	REQUIRED ACTION
Opportunistic or serious infection	Hold until evaluated and resolved.
JCV seroconversion or markedly rising index	Pause while re-counseling and re-stratifying; some patients continue with intensified MRI.
Planned switch to another DMT	Coordinate washout deliberately — unplanned gaps risk rebound.

B. Discontinue permanently

CRITERION	REQUIRED ACTION
PML confirmed or strongly suspected	Discontinue immediately; anticipate IRIS as surveillance recovers — corticosteroid management under specialist care.
Anaphylaxis or serious hypersensitivity	Discontinue permanently.
Persistent neutralizing antibodies	Discontinue (efficacy lost).
Patient elects to stop after risk counseling	Mandatory transition plan — rebound relapses peak months 3–6 off drug.

Section 5 — Notes & Practical Points

- ☐ PML risk is quantifiable and changes over time — recalculate with the patient at least every 6–12 months using duration, JCV index, and prior immunosuppression.
- ☐ Natalizumab withdrawal without follow-on therapy is one of the highest-risk maneuvers in MS care: severe rebound disease activity and IRIS are both well described.

Prepared November 2026 by Madison Neurology LLC.

This document is an educational compilation and does not reproduce the complete prescribing information. Verify every element against the current FDA label and applicable REMS requirements before clinical use.

- Current U.S. prescribing information via NIH DailyMed — https://dailymed.nlm.nih.gov/dailymed/
- FDA Drugs@FDA database — https://www.accessdata.fda.gov/scripts/cder/daf/
- FDA drug safety and availability updates — https://www.fda.gov/drugs/drug-safety-and-availability

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Questions about infusion referrals: call 608 403 0000. Neurology Care 7 days a Week. Because Your Brain Matters.