TYSABRI® (natalizumab) Risk Management Plan

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TYSABRI® Risk Management Plan

- TYSABRI Regulatory Background
- Risk Management (RiskMAP) Goals, System and Tools
- RiskMAP Evaluation
- RiskMAP Challenges

TYSABRI® (natalizumab) History

November 2004

- TYSABRI approved in US for relapsing forms of multiple sclerosis (MS)

February 2005

- 2 cases of progressive multifocal leukoencephalopathy reported
- Voluntary suspension of TYSABRI, safety evaluation begun

September 2005

- Safety evaluation completed, sBLA filed with FDA

March 2006

- FDA Advisory Committee recommends re-introduction of TYSABRI

April 2006

- CHMP recommends TYSABRI approval in Europe

June 5, 2006

- FDA re-approval and CHMP approval

July 2006

- US re-introduction and EU launch

Disease-Modifying Therapies Currently Approved for Relapsing Forms of MS

Treatment	Reduction in Relapse Rate	Reduction in Disability Progression	Side Effects
IFNβ Products (e.g. AVONEX®, Rebif, Betaseron)	29% – 34%	24% – 37% **	♦ Injection-site reactions ♦ Flu-like symptoms ♦ Depression ♦ Hepatotoxicity
Copaxone	29%	Not statistically significant	♦ Injection-site reactions ♦ Lipoatrophy ♦ Acute systemic reactions
TYSABRI®	68%	42% – 54%	♦ Risk of PML ♦ Infusion reactions ♦ Headache ♦ Fatigue

Note: Results from separate clinical studies cannot be directly compared.
**Only IM IFNβ-1a and SC IFNβ-1a have shown statistically significant effects on disability progression.

Central Role of MS Patients in the Return of TYSABRI

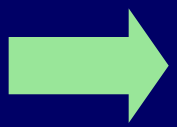
FDA Advisory Committee Meeting on TYSABRI®

TYSABRI Risk Management Plan

TYSABRI Risk Management Goals

- Risk Minimization Goals
  - Promote informed benefit-risk decisions
  - Minimize the risk of PML
  - Potentially minimize death and disability due to PML

- Risk Assessment Goals
  - Determine the incidence and risk factors for PML
  - Assess long-term safety in clinical practice



Evaluation and Enhancements

TYSABRI Revised Labeling: New Indication Statement

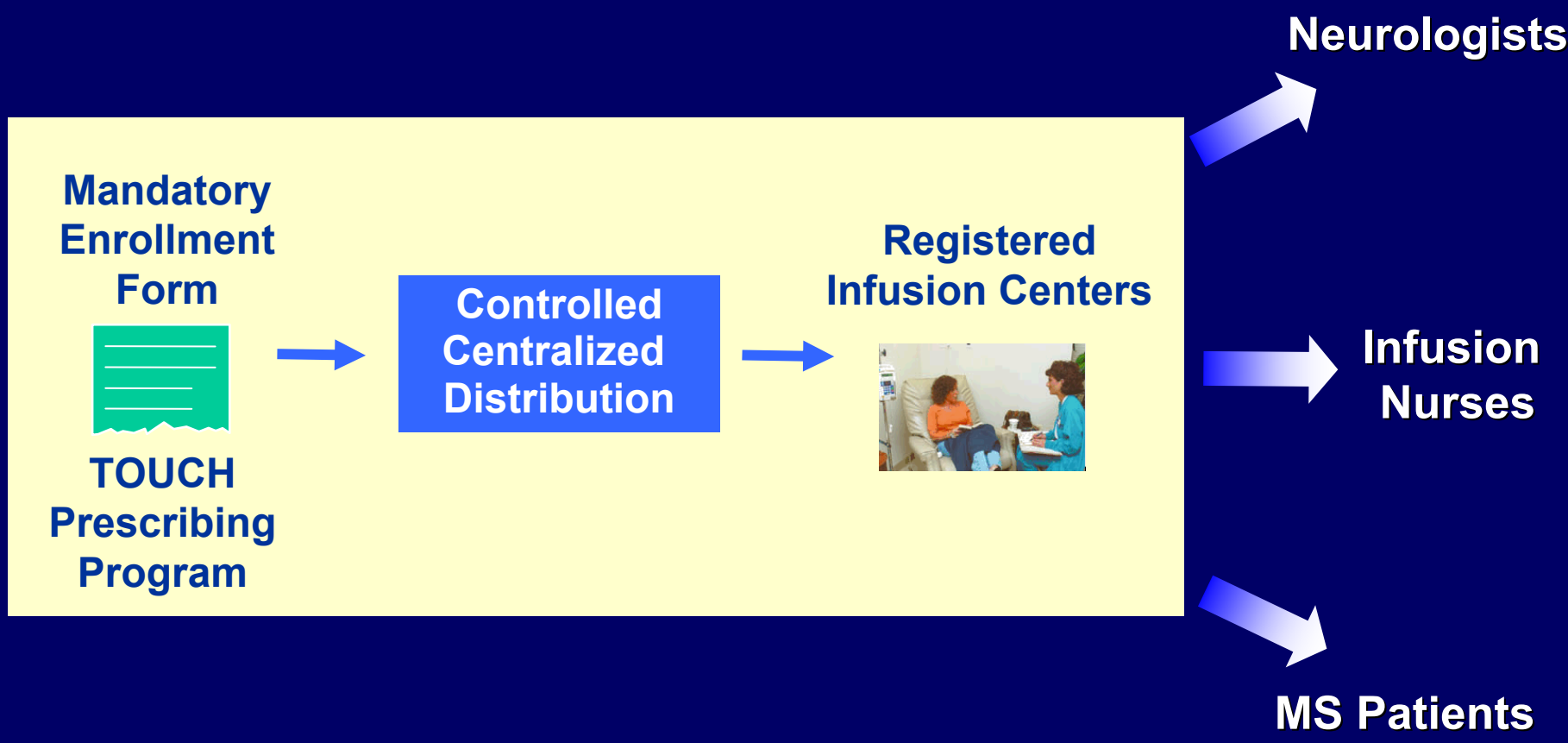
- TYSABRI is indicated as monotherapy for the treatment of patients with relapsing forms of MS to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations

- Because TYSABRI increases the risk of PML, an opportunistic viral infection of the brain that usually leads to death or severe disability, TYSABRI is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, alternate MS therapies

TYSABRI Revised Labeling: New Boxed Warning

- TYSABRI increases the risk of PML, an opportunistic viral infection of the brain that usually leads to death or severe disability
- Although the cases of PML were limited to patients with recent or concomitant exposure to immunomodulators or immunosuppressants, there were too few cases to rule out the possibility that PML may occur with TYSABRI monotherapy
- Healthcare professionals should monitor patients for any new signs or symptoms that may be suggestive of PML
  - Dosing should be withheld immediately at the first signs or symptoms suggestive of PML
  - Evaluation should include brain MRI and CSF for JC viral DNA

TYSABRI Risk Minimization System



Prescriber-Patient Acknowledgement on Enrollment Form

- Records informed benefit-risk decision before start of therapy
- Physician signs:
  - Is aware of PML risk
  - Has discussed risks and benefits with patient
  - Patient appropriate for TYSABRI
- Patient signs:
  - Has read Medication Guide
  - Has discussed risks and benefits with physician
  - Will report new or worsening neurological symptoms to their physician

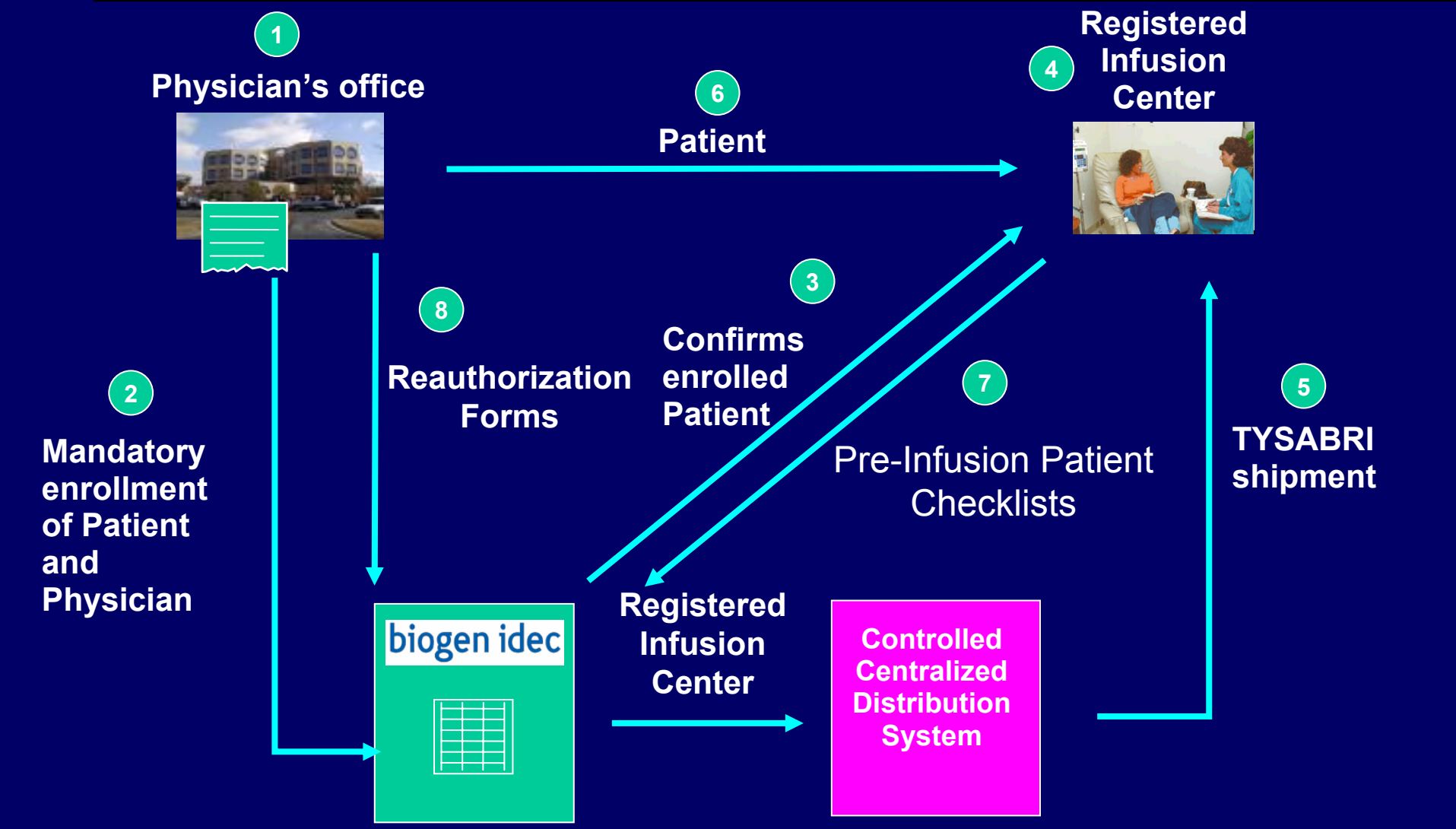
Prescriber Requirements

- Must report any PML, serious opportunistic infection, or death to Biogen Idec
- Must complete a Patient Reauthorization Questionnaire on every patient every 6 months and submit to Biogen Idec:
  - Patient vital status, PML, and other serious opportunistic infections
  - Any concurrent immunomodulatory or immunosuppressant medications
  - Reauthorization of TYSABRI dosing for next 6 months
- Must complete Discontinuation Questionnaire 6 months after patient's last dose and submit to Biogen Idec

Infusion Center Requirements

- TYSABRI use only in registered infusion centers
  - Educational training of infusion nurses
  - Infusion center attests to follow risk management requirements
- Dosing only to patients enrolled in TOUCH Prescribing Program
- Medication Guide to patient with every dose
- Mandatory completion of Pre-Infusion Patient Checklist for each patient before each dose
  - Screens patient for new or worsening neurological symptoms
  - Reinforces use as a monotherapy and not in immunocompromised patients
- Real-time submission of Pre-Infusion Patient Checklists to Biogen Idec
  - to monitor infusion center compliance and
  - to track TYSABRI dosing on patient-specific basis

TYSABRI Risk Minimization System



TOUCH Prescribing Program Evaluation

TYSABRI Exposure Worldwide

- In commercial use and clinical trials, ~12,000 patients on TYSABRI therapy worldwide
  - US: ~8,300 patients dosed
  - Europe: ~3,200 patients dosed
  - 1,000 patients on TYSABRI in clinical trials
- Worldwide cumulative exposure of ~21,000 patients

Note: Tysabri metrics as of 23 May 2007

TOUCH Enrollment (US)

- ~11,000 patients enrolled in TOUCH, of which ~8,300 patients exposed; median of 4 doses
  - ~3% naïve to any MS therapy
- ~1,700 physicians have enrolled patients
- ~1,700 infusion sites trained and authorized

Note: Tysabri metrics as of 23 May 2007

TOUCH Process Metrics

- 99.9% of infusions are to patients enrolled in the program
  - Patients and prescribers informed about risk
- 96.8% of patients with no concurrent immunomodulatory or immunosuppressant therapies
  - TYSABRI prescribed as monotherapy, according to label
- 99.9% of 10,126 drug shipments shipped to authorized infusion sites
- 99.9% of 38,898 Pre-infusion Patient Checklists received
  - Reinforces importance of clinical vigilance in early detection of PML

Excellent Program Compliance

Note: TYSABRI metrics as of 23 May 2007

TOUCH Surveys of Prescribers and Infusion Nurses

- High awareness of PML risk
  - 99% of prescribers know of increased risk of PML
  - 100% of nurses know TYSABRI should be administered only to enrolled patients
- Majority understand key components of TOUCH
  - 98% of prescribers know to report PML
  - 99% of nurses know to contact prescriber if patient reports new neurological symptoms

High Level of PML Awareness

Through 23 February 2007

TYSABRI Safety Outcomes

- No new confirmed cases of PML or other serious opportunistic infection
- Post-marketing safety profile consistent with clinical trials

Note: Tysabri metrics as of 23 May 2007

Challenges with TOUCH Prescribing Program

Implementation of Complex Program

- Successful implementation
  - High program compliance
  - Use in appropriate patients, as monotherapy
  - High awareness of PML risk

- Key success factors:
  - Motivated patients and prescribers
  - MS is serious disabling disease; high unmet need for more effective therapies
  - Biogen Idec has extensive experience in MS community
  - Leveraged existing patient and physician support infrastructure for AVONEX (interferon beta-1a)
  - Applied significant company resources
  - Intensive education and training of patients and healthcare professionals

Challenges in Communication

- Under SubPart E, ability to provide up-to-date safety data is limited
  - Prescribers and patients expect latest safety data
  - Communication materials, including non-promotional safety data, must be pre-reviewed by Agency, leading to delay

- Benefit-risk message not balanced
  - 77% of patients do not understand TYSABRI benefit
  - Need to consistently communicate both benefit and risk information for products with RiskMAPs
  - May lead patients to consider alternative, unproven therapies for MS

Emergence of Unintended Consequences

- TYSABRI is utilized more frequently in large care centers, compared to small neurology practices
- Many physicians say program may prevent patient access because of administrative burden to their practice
- Physicians express liability concerns regarding Prescriber-Patient Acknowledgement
- Leads to limitations in patient access to TYSABRI
- Opportunity to streamline redundancies while protecting public health

Importance of Clear Mechanism to Engage FDA in RiskMAP Evaluation

- Process for RiskMAP evaluation is unique and dynamic
- Requires interaction with many FDA divisions
- No clear “rules of engagement” with FDA once RiskMAP is approved (e.g. no PDUFA timelines)
- Single point-of-contact at FDA may facilitate these interactions
- Need clear mechanisms and timeframes to engage FDA in on-going evaluation and refinements to RiskMAP

TOUCH Prescribing Program Summary

- TYSABRI confers unique benefit in relapsing MS - a serious and disabling disease
- RiskMAP successfully implemented
- RiskMAP evaluation and enhancement requires new mechanism for FDA interactions post-approval
- Importance of communicating real-time safety data and balanced benefit-risk information to public