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# **TYSABRI**

# **Risk Management Plan**

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# Presentation Outline

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- ◆ Overview and Goals of Plan
- ◆ Risk Minimization Plan
- ◆ Risk Assessment Plan
- ◆ Evaluation of Plan
- ◆ Benefit-Risk Considerations

# TYSABRI Risk Management Plan Development

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- ◆ Based on FDA Guidance document and ongoing dialogue with FDA
- ◆ Present updated version of plan
- ◆ Careful review of risk management plans with other drugs

# TYSABRI Risk Management Plan Development

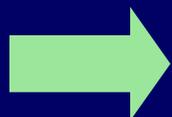
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- ◆ Developed based on feedback from many neurologists, infusion nurses, and MS patients
  - Neurology expert panels and advisory boards
  - Infusion nurse and MS patient focus groups and surveys
- ◆ Minimize risk without creating unintended consequences that may obstruct patient access

# **TYSABRI Risk Management Goals**

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- ◆ 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**

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# Risk Minimization Plan

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## Important Features of TYSABRI Treatment

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- ◆ Monthly infusions by healthcare professional
- ◆ Prescribed by small group of neurology specialists
- ◆ Neurologists best qualified specialists to manage PML

# Risk Minimization Plan

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- ◆ Revised Labeling
- ◆ Risk Minimization System

# TYSABRI Revised Labeling: Key Concepts in New Boxed Warning

- ◆ TYSABRI is associated with increased risk of PML which causes death or severe disability
- ◆ Warn against concurrent use with immunosuppressants (eg, azathioprine) or immunomodulators (eg, interferon-beta)
- ◆ Indicated *only* for relapsing MS
- ◆ Healthcare professionals should be alert to any signs or symptoms that may be suggestive of PML
  - Dosing should be suspended immediately at the first signs or symptoms suggestive of PML
  - Evaluation should include brain MRI and CSF for JC viral DNA

## **TYSABRI Revised Labeling: Additional Warnings**

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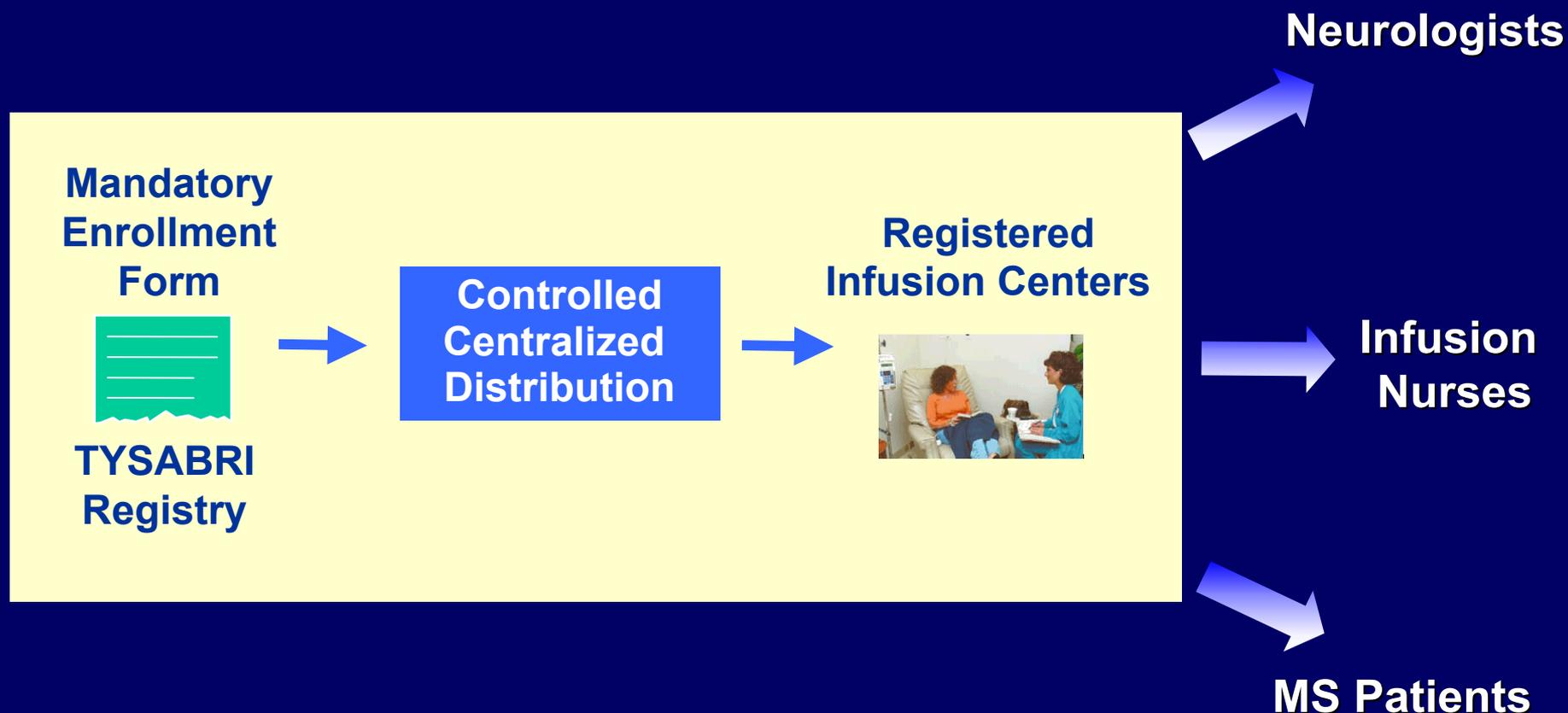
- ◆ An MRI scan should be obtained prior to initiating  
TYSABRI
- ◆ Contraindicated in patients who are immunocompromised

# Risk Minimization Plan

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- ◆ Revised Labeling
- ◆ Risk Minimization System

# TYSABRI Risk Minimization System



# Patient-Physician Acknowledgement on Enrollment Form

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- ◆ 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

# Infusion Center Requirements

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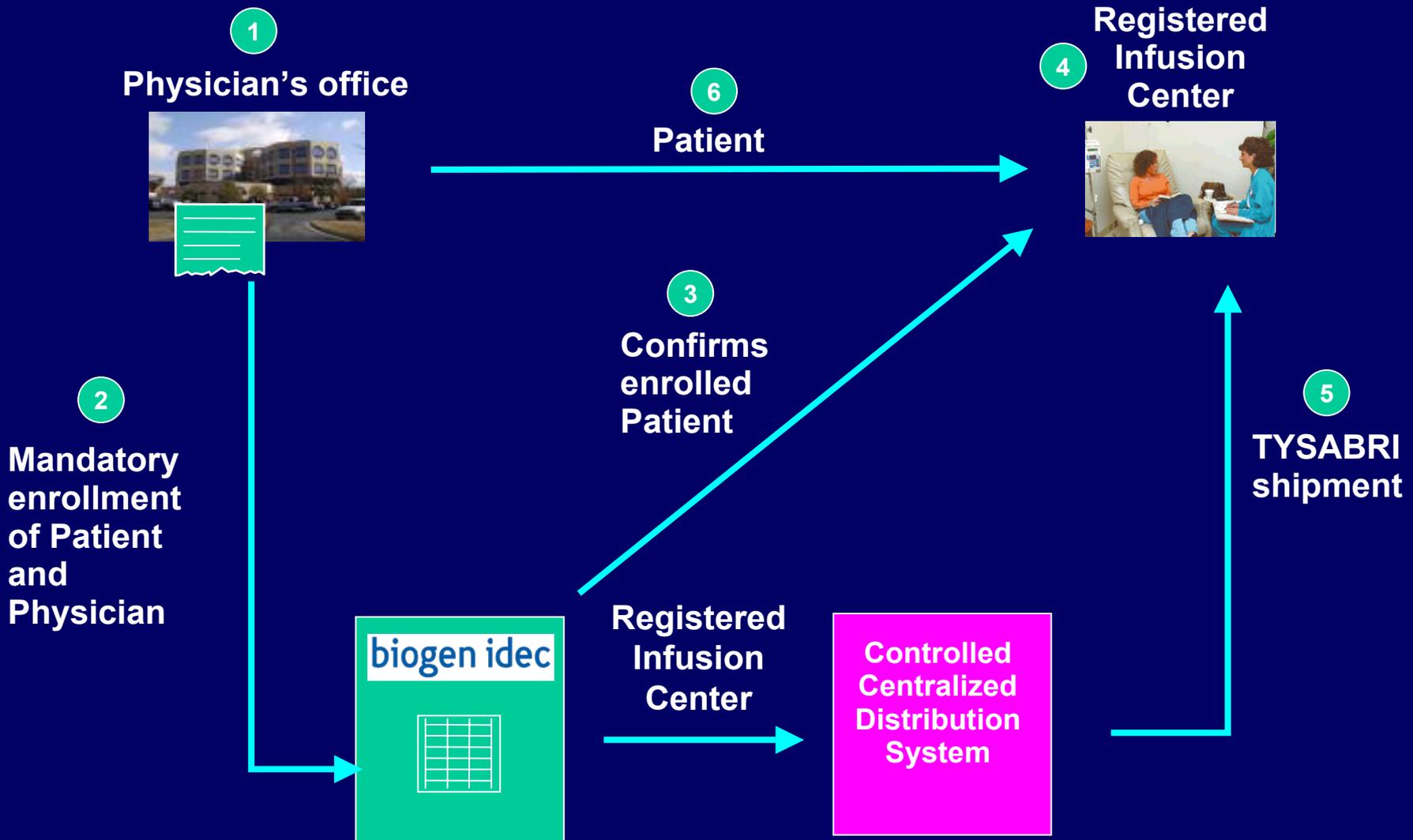
- ◆ TYSABRI use only in registered infusion centers
  - Educational training of infusion nurses
  - Infusion center attests to follow risk management requirements
- ◆ Dosing only to patients enrolled in TYSABRI Registry
- ◆ Medication Guide to patient with every dose
- ◆ Documentation in TYSABRI Infusion Log
- ◆ Infusion centers will be audited by Biogen Idec
  
- ◆ **Completion of Patient Checklist before each dose**

# Pre-Infusion Patient Checklist

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- ◆ Designed based on feedback from neurologists
- ◆ Screens patient for new or worsening neurologic symptoms
  - If symptoms are detected, the physician will be immediately contacted and dosing will be suspended
- ◆ Administered prior to each infusion in each patient
  - By neurologist or neurologist's nurse in office or by phone OR
  - By infusion nurse in infusion center
  - Appropriate for use in multiple clinical practice settings
- ◆ Facilitates close clinical follow-up of all patients
- ◆ Reinforces use as monotherapy and not in immunocompromised patients

# TYSABRI Risk Minimization System



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# Risk Assessment Plan

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# Commitment to Further Study TYSABRI Safety

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## Major Post-Marketing Studies

- ◆ TYSABRI Registry
- ◆ TYSABRI Observational Cohort Study

## Additional Studies

- ◆ Re-dosing studies
- ◆ PML epidemiological studies
- ◆ Immune function study
- ◆ Non-clinical studies

# TYSABRI Registry

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## Purpose:

To determine incidence and risk factors in TYSABRI-treated patients for PML and other serious opportunistic infections

- ◆ Mandatory enrollment of physicians and patients
- ◆ Physicians to report any PML event to Biogen Idec
- ◆ Physicians queried on every patient every 6 months on:
  - PML, other serious opportunistic infections, death of any cause, TYSABRI discontinuation
  - Patients remain in Registry for minimum 6 months after last dose
- ◆ Collect all spontaneously reported adverse events

## **TYSABRI Registry (Cont'd)**

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- ◆ Follow-up of patient deaths through National Death Index and collection of death certificates
- ◆ Non-compliance will result in “de-enrollment”
- ◆ Provides intense safety surveillance and tracking of all patients, far exceeding routine pharmacovigilance

## TYMABRI Registry (Cont'd)

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If PML occurs:

- ◆ Thorough data collection related to case
- ◆ Analysis of any PML case
- ◆ Pre-defined criteria for PML
- ◆ Expedited reporting to the FDA
- ◆ Ongoing assessment of benefit-risk

# TYSABRI Observational Cohort Study

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## Purpose:

Evaluation of TYSABRI long-term safety in clinical practice setting

- ◆ Subset of patients in TYSABRI Registry will enroll into this voluntary observational cohort study
- ◆ 5000 MS patients worldwide (3000 in US) followed for 5 years
- ◆ Powered to detect rare events with incidence of 0.06%
- ◆ Collects all serious adverse events and concomitant immunomodulatory and immunosuppressant therapies
- ◆ Assess risk of serious infections and malignancies
- ◆ Investigate potential signals of unanticipated adverse events

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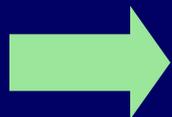
# Evaluation of Risk Management Plan

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## Evaluation of Risk Management Plan

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- ◆ Monitor success of risk management plan
- ◆ Includes analysis of data from TYSABRI Registry
- ◆ Share data with FDA every 3 months
- ◆ If needed, implement rapid corrective actions
  - Labeling changes
  - Improvements in risk minimization system and tools



**Evaluation and Enhancements**

# Summary:

## **TYSABRI Risk Management Plan**

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- ◆ Goals: To inform and minimize risk of PML
  - Mandatory registration of all prescribers and patients
  - Monthly screening of patients
  - Controlled, centralized distribution
  - Use only in registered infusion centers
- ◆ Ongoing assessment of PML risk and overall safety
- ◆ Evaluation plan to monitor success of risk management
- ◆ Appropriate use without unnecessary burden to physicians or barriers to patient access

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# **Benefit-Risk Considerations**

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# Benefit-Risk Considerations

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- ◆ MS is a devastating, progressively disabling neurologic disease with high unmet need
- ◆ TYSABRI is a highly effective therapy
- ◆ Benefit consistent in broad range of sub-groups
- ◆ PML is a rare but serious risk
- ◆ Comprehensive risk management plan to minimize and assess this risk
- ◆ Favorable benefit-risk profile

# Appropriate Use of TYSABRI

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## Use Conditions

Relapsing MS Patients:

- Only as monotherapy
- Not immunocompromised
- Enrolled in TYSABRI Registry
- Fully informed about PML risk

## Patient Selection

Relapsing MS Patients:

- With disease activity on current therapy, or
- Intolerant of current therapy, or
- With high disease activity, or
- Others deemed appropriate based on individual benefit-risk assessment