I. PURPOSE
The purpose of a Standard Operating Procedure (SOP) is to define best practices of how MS patients will be managed in the clinic using Rituxan (rituximab).

II. SCOPE
This SOP is intended for us by all Neuroimmunologic clinicians within the UCD/UCH Neurology Department when prescribing Rituxan, in order to minimize risk associated with the use of this medication.

III. THERAPEUTIC DRUG BACKGROUND
Rituxan (rituximab) is an anti-CD20 monoclonal antibody which specifically targets and binds to CD20 expressed on naïve and memory B lymphocytes. It results in the depletion of peripheral CD20 expressing B lymphocytes, and reduces T lymphocytes. CD20 expressing B cells are depleted through antibody dependent cytotoxicity, complement mediated destruction, and antibody mediated apoptosis. The primary mechanism of action of this therapeutic is through the depletion of CD20 expressing B lymphocytes; however the observed reduction in T lymphocytes may also contribute. (http://www.rituxan.com/hem/hcp/non-hodgkin/post-induction/prima/index.html); (UCD Translational Lab)

IV. DOSING
Baseline Dosing:
- Rituximab (Rituxan) dose intravenous 1000mg once

Maintenance Dosing:
- Rituximab (Rituxan) dose intravenous 500mg every 6 months

Pediatric Dosing:
- 375 mg/m2 (body surface area)
  BSA = [Height(cm) x Weight(kg)]/3600½ (Maximum 1000mg)

V. SAFETY ASSESSMENTS
A. Relatively Contraindicated For:
- Patients who are immunosuppressed
- Use with care in patients considering pregnancy within 2 years.
- Patients with a comorbidity of HIV or Viral Liver Disease

B. Clinical Assessments:
- Patient Visit (every 3 months; every 6 months after year 1 if stable) includes:
  - Physical Exam
  - Comorbidity evaluation (incl. obesity, diabetes, hypertension…)
  - Verify Conmeds (prescription medications)
- PROs every 12 months

C. Baseline Assessments
LABS:
- Pregnancy Serum
- CBC w/ Autodiff
- Complete Metabolic Panel
- Hepatitis B Core Antibodies
- Hepatitis B Surface Antibody
- Hepatitis B Surface Antigen
- Hepatitis C Virus Antibody
- HIV 1 & 2 Antibody (order HIV ½ Antibody/Antigen in Epic)
- Immunoglobulin G
- Immunoglobulin M
Immunoglobulin A
CD19 (order Anti-CD20 monitoring panel in Epic)
CD3/CD4/CD8 (order T-cell panel in Epic)
Vitamin D
JCV Status

**RADIOLOGY:**
Brain MRI w/wo Contrast Baseline (order MR Brain Multiple Sclerosis in Epic) within 3 mos of initiating drug (MRI after drug initiation ideal) or as soon thereafter when possible

**D. Follow-up Assessments**

**LABS:**
- Pregnancy Serum (if suspected)
- CBC w/ Autodiff (prior to infusion)
- CMP (prior to infusion)
- Hepatitis B Core Antibodies (repeat every 2 years)
- Hepatitis B Surface Antibody (repeat every 2 years)
- Hepatitis B Surface Antigen (repeat every 2 years)
- Hepatitis C Virus Antibody (repeat every 2 years)
- HIV ½ Antibody (repeat every 2 years)
- Immunoglobulin G (repeat annually)
- Immunoglobulin M (repeat annually)
- Immunoglobulin A (repeat annually)
- Anti-CD20 monitoring panel (prior to infusion)
- Vitamin D (repeat every 6 months)
- JCV Status (repeat every 6 months)

**RADIOLOGY:**
Brain MRI w/wo Contrast (order MR Brain Multiple Sclerosis in Epic) repeat within months 24 – 30 after initiation of drug and at onset of new neurologic symptoms suggesting either MS or PML.

**VI. APPLICABLE REGULATIONS AND GUIDELINES**
**A. PDR (http://www.pdr.net)**

**VII. DEFINITIONS**
**A. Acronyms**
- PRO: Patient Reported Outcomes
- MS: Multiple Sclerosis
- PML: Progressive Multifocal Leukoencephalopathy
- PDR: Physician’s Desk Reference

**VIII. REFERENCES TO OTHER APPLICABLE SOPs**
N/A

**IX. ACCOUNTABILITY**
X. The following clinicians will be responsible for using this SOP when selected for treating patients with MS:
- Timothy Vollmer, MD
- John Corboy, MD
- Augusto Miravalle, MD
- Jeffrey Bennett, MD PhD
- Teri Schreiner, MD
- Enrique Alvarez, MD PhD
The PRO Project Manager is responsible for:
- Creating/Maintaining this SOP on a routine basis
- Convening the PRO team to review any relevant changes to this SOP

XI. POLICY
This SOP is for use as a treatment option for patients with Multiple Sclerosis.

XII. REFERENCES
http://www.rituxan.com
http://www.nationalmssociety.org
http://www.pdr.net

XIII. REVIEW
Staff responsible for authoring, reviewing and revising this SOP is the PRO Project Manager.

XIV. DOCUMENT HISTORY
This section lists each revision and version of the SOP. It also supplies a reference to the specific SOP Revisions form that lists the changes made during each revision.

<table>
<thead>
<tr>
<th>Version</th>
<th>Description</th>
<th>Reason for Revision</th>
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<tbody>
<tr>
<td>2013-12-15</td>
<td>MS Rituxan</td>
<td>Creation</td>
</tr>
</tbody>
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XV. Statement of Consensus
The above listed providers have agreed through consensus of the majority that this SOP will be utilized when prescribing Rituxan for MS patients.