curative

TITLE:	MULTIPLE SCLEROSIS POLICY
POLICY #:	MM-PNP-028
VERSION #:	01
DEPARTMENT:	UTILIZATION REVIEW
ORIGINAL EFFECTIVE DATE:	12/01/2023
CURRENT REVISION DATE:	N/A

1. PURPOSE

Brand Selection for Medically Necessary Indications

Lemtrada
As defined in Curative commercial policies, health care services are not medically necessary when they are more costly than alternative services that are at least as likely to produce equivalent therapeutic or diagnostic results. Lemtrada (alemtuzumab) is more costly to Curative than other targeted immune modulators for the treatment of relapsing forms of multiple sclerosis (MS). There is a lack of reliable evidence that Lemtrada (alemtuzumab) is superior to the lower cost alternatives. Therefore, Curative considers Lemtrada (alemtuzumab) to be medically necessary only for members who have a contraindication, intolerance or ineffective response to an adequate trial of Tysabri.

****Intolerance is defined as intolerable side effects despite optimized management strategies.**

****Failure of an adequate trial of therapy for multiple sclerosis is defined as follows:**

- the member has increasing relapses, defined as two or more relapses in a year, or one severe relapse associated with either poor recovery or MRI lesion progression; or
- the member has lesion progression by MRI (increased number or volume of gadolinium-enhancing lesions, T2 hyperintense lesions or T1 hypointense lesions); or
- the member has worsening disability (sustained worsening of Expanded Disability Status Scale [EDSS] score or neurological examination findings).

2. SCOPE

Medical and Pharmacy UM Departments

3. DEFINITIONS

N/A

4. RESPONSIBILITIES

N/A

5. POLICY

Requires Precertification:

Precertification of multiple sclerosis medications are required of all Curative participating providers and members in applicable plan designs.

Alemtuzumab (Lemtrada)

Prescriber Specialties

This medication must be prescribed by or in consultation with a neurologist.

Criteria for Initial Approval

Curative considers alemtuzumab (Lemtrada) medically necessary when criteria are met:

- **First Course** - relapsing forms of multiple sclerosis

  For members with a diagnosis of a relapsing form of multiple sclerosis (MS) (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse) who have had an inadequate response to two or more drugs indicated for MS; ***or***

- **Subsequent Courses** - relapsing forms of multiple sclerosis

  For members with a diagnosis of a relapsing form of MS (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse) who have completed at least one previous course of therapy and treatment will start at least 12 months after the last dose of the prior treatment course.

- **Other**
  - Members will not use Lemtrada concomitantly with other disease modifying multiple sclerosis agents (**Note:** Ampyra and Nuedexta are not disease modifying).
  - Authorization may be granted for pediatric members less than 18 years of age when benefits outweigh risks.

Curative considers all other indications as experimental and investigational (for additional information, see Experimental and Investigational section).

Intravenous Steroid Treatment

Curative considers intravenous steroid therapy medically necessary for either of the following indications:

- Treatment of acute exacerbations of multiple sclerosis (MS) when the acute relapse is characterized by functionally disabling symptoms with documented evidence of neurological impairment (persons who have previously responded in a relapse phase are more likely to do so in the future); *or*
- Use of intermittent pulse dose corticosteroids as a maintenance treatment for MS to delay disease progression. In many cases, members can be treated in the outpatient setting.

Curative considers hospital admission for intravenous steroid therapy medically necessary for the treatment of an acute exacerbation of MS that results in *any* of the following severe neurological deficits:

- Acute cerebral symptoms with severe loss of intellectual capacity; *or*
  - Acute epileptic seizure(s); *or*

- Acute fulminant MS characterized by headache, vomiting, convulsions and eventually coma, with severe compromise of functioning of the central nervous system; *or*
- Acute pseudobulbar palsy; *or*
- Acute quadriplegia; *or*
- Acute transverse myelitis (or Brown-Sequard syndrome) with loss of function below the level of a suspected lesion in the spinal cord; *or*
- Acute visual loss.

An inpatient stay may also be considered medically necessary for persons who have had previous complications from high dose intravenous steroids that justify an inpatient admission.

Mitoxantrone Intravenous Injection

Prescriber Specialites

This medication must be prescribed by or in consultation with a neurologist.

Criteria for Initial Approval

Curative considers mitoxantrone intravenous injection medically necessary for members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting, secondary progressive, and progressive relapsing disease. **Note**: Mitoxantrone is not indicated in the treatment of primary progressive MS.

Curative considers all other indications as experimental and investigational (for additional information, see Experimental and Investigational and Background sections).

Continuation of Therapy

Curative considers continuation of mitoxantrone intravenous injection medically necessary for members who meet initial criteria and are experiencing disease stability or improvement, and there is no evidence of unacceptable toxicity while receiving mitoxantrone therapy.

Ocrelizumab (Ocrevus)

Prescriber Specialties

This medication must be prescribed by or in consultation with a neurologist.

Criteria for Initial Approval

Curative considers ocrelizumab (Ocrevus) medically necessary for the following indications when criteria are met:

- Relapsing Forms of Multiple Sclerosis - for members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse); *or*
- Clinically Isolated Syndrome (CIS) - for treatment of clinically isolated syndrome of multiple sclerosis; *or*
- Primary Progressive Multiple Sclerosis - for treatment of primary progressive multiple sclerosis.

Curative considers all other indications as experimental and investigational (for additional information, see Experimental and Investigational and Background sections).

Continuation of Therapy

Curative considers continuation of ocrelizumab (Ocrevus) therapy medically necessary for all indications when members are experiencing disease stability or improvement while receiving Ocrevus.

Other

- Members will not use Ocrevus concomitantly with other disease modifying multiple sclerosis agents; **Note:** Ampyra and Nuedexta are not disease modifying;
- Authorization may be granted for pediatric members less than 18 years of age when benefits outweigh risks.

Plasma Exchange / Plasmapheresis

Plasma exchange (PLEX) / plasmapheresis is considered medically necessary for members with acute, severe neurological deficits caused by MS who have a poor response to treatment with high-dose glucocorticoids.

Ublituximab-xiiy (Briumvi)

Prescriber Specialties

This medication must be prescribed by or in consultation with a neurologist.

Criteria for Initial Approval

Curative considers ublituximab-xiiy (Briumvi) medically necessary for the following indications when criteria are met:

- Relapsing forms of multiple sclerosis - for members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse); *or*
- Clinically isolated syndrome (CIS) - for the treatment of clinically isolated syndrome of multiple sclerosis.

Curative considers all other indications as experimental and investigational.

Continuation of Therapy

Curative considers continuation of ublituximab-xiiy (Briumvi) therapy medically necessary for members who are experiencing disease stability or improvement while receiving Briumvi.

Other Criteria

- Members will not use Briumvi concomitantly with other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).
- Authorization may be granted for pediatric members less than 18 years of age when benefits outweigh risks.

For purpose of this policy, failure of an adequate trial of therapy for multiple sclerosis is defined as follows:

- The member has increasing relapses (defined as two or more relapses in a year, or one severe relapse associated with either poor recovery or MRI lesion progression); *or*
- The member has lesion progression by MRI (increased number or volume of gadolinium-enhancing lesions, T2 hyperintense lesions or T1 hypointense lesions); *or*
- The member has worsening disability (sustained worsening of Expanded Disability Status Scale (EDSS) score or neurological examination findings).

Intolerance is defined as intolerable side effects despite optimized management strategies.

Experimental and Investigational

Curative considers the following interventions experimental and investigational for MS (not an all-inclusive list):

- Alpha-interferon
- Anti-T-cell monoclonal antibodies other than natalizumab (Tysabri, Antegren)
- Anti-lymphocyte globulin
- APOE genotyping
- Balloon angioplasty / balloon venoplasty / venous angioplasty with or without stent placement (chronic cerebrospinal venous insufficiency (CCSVI) treatment)
- Brainstem auditory evoked response for diagnosing MS
- Cannabis and cannabinoids
- Cerebrospinal fluid levels of neurofilament as a biomarker of MS
- Clemastine fumarate for the treatment of chronic demyelinating injury in MS
- Cooling garment
- Cosyntropin (Cortrosyn)
- Cyclosporine (Sandimmune)
- Dietary interventions (e.g., gluten-free diets, low fat diets, linoleate supplementation to diet, and dietary regimens with polyunsaturated fatty acids)
- Electronystagmography (in the absence of vertigo or balance disorder)
- Erythropoesis stimulating agents (unless criteria are met in CPB 0195 - Erythropoiesis Stimulating Agents or CPB 0195m - Erythropoiesis Stimulating Agents [Medicare])
- Estrogen receptor beta ligands
- Ferritin/iron status (blood or CSF) for the diagnosis of MS
- Functional electrical stimulation (FES) cycling
- Gamma-interferon
- gMS®DX and gMS®Pro EDSS tests for the diagnosis of MS
- Hyperbaric oxygen

- Intravesical vanilloids (e.g., capsaicin and resiniferatoxin) for the treatment of neurogenic lower urinary tract dysfunction in individuals with MS
- IL-2-toxin
- IL-10
- IL-16
- Interleukin-1 gene polymorphisms testing
- IVIG for Multiple Sclerosis (relapsing MS and progressive MS) (see CPB 0206 - Parenteral Immunoglobulins or CPB 0206m - Parenteral Immunoglobulins [Medicare])
- Mesenchymal stem cell therapy
- Mesenchymal stromal cell-derived neural progenitors
- Methotrexate
- MTHFR testing for MS
- Myelin basic protein peptides
- Myxovirus resistance protein A (MxA) as a biomarker for MS relapse/treatment response
- Naltrexone
- Neurite orientation dispersion and density imaging (NODDI) for evaluation of MS
- Non-invasive brain stimulation for improvement of cognitive and motor functions in MS
- Non-pharmacological interventions (biofeedback, hydrotherapy, hypnosis, reflexology, transcranial direct stimulation, transcranial random noise stimulation, and transcutaneous electrical nerve stimulation) for the treatment of chronic pain in MS
- Optical coherence tomography angiography measurements for MS
- Optical coherence tomography for screening of member receiving fingolimod (Gilenya) for macular edema (see CPB 0344 - Optic Nerve and Retinal Imaging Methods)
- Oral myelin (Myloral)
- Osteopontin as a biomarker for MS
- Otoacoustic emissions (in the absence of signs of hearing loss)
- Photopheresis (see CPB 0241 - Extracorporeal Photochemotherapy (Photopheresis))
- Plasmapheresis for chronic or secondary progressive MS (maintenance therapy)
- Procarin (transdermal histamine)
- Prolactin
- Pulsed magnetic field therapy
- PUVA (psoralen ultraviolet light)
- Retinal nerve scanning for screening/monitoring persons on fingolimod (Gilenya)
- Ribavirin

- Serum neurofilament as a marker of neuroaxonal injury in early MS and for monitoring disease activity
- Sildenafil
- Statins
- Stem cell transplantation (see CPB 0606 - Stem Cell Transplant for Autoimmune Diseases and Miscellaneous Indications
- T-cell receptor therapy
- T-cell vaccination
- Total lymphoid irradiation
- Transcranial brain sonography for predicting disease progression in MS
- Transforming growth factor (TGF)-beta
- Tumor necrosis factor antagonists
- Tympanometry (in the absence of hearing loss)
- Virtual reality-based therapy for improvement of balance and reduction of fear of falling in individuals with MS.

Curative considers assays of neutralizing antibodies (NABs) against interferon beta (Betaseron) to be experimental and investigational because its clinical value has not been established.

Curative considers measurements of hematopoietic stem and progenitor cells counts as a biomarker of responsiveness to natalizumab experimental and investigational because its clinical value has not been established.

Curative considers determination of the expression of the splice variants of the tumor necrosis factor-related apoptosis inducing ligand (TRAIL) and its receptors as a biomarker of responsiveness to interferon-beta experimental and investigational because its clinical value has not been established.

Concomitant Use

Curative considers alemtuzumab (Lemtrada), cladribine (Mavenclad), dimethyl fumarate (Tecfidera), fingolimod (Gilenya), glatiramer acetate (Copaxone, Glatopa), interferon beta, natalizumab (Tysabri), ocrelizumab (Ocrevus), siponimod (Mayzent) and/or teriflunomide (Aubagio) used concomitantly with other disease modifying multiple sclerosis agents **(Note**: **Ampyra and Nuedexta are not disease modifying)** to be experimental and investigational because the clinical value has not been established.

6. PROCEDURE

N/A

7. TRAINING REQUIREMENT

- All Curative Medical and Pharmacy UM associates are responsible for reading and comprehending this procedure. Employees are also responsible for contacting management or Privacy and Compliance with any questions or concerns regarding the information contained within this procedure.

8. ENFORCEMENT

Violations of this controlled document will cause the imposition of sanctions in accordance with the Curative sanctions-controlled document. This may include verbal/written warning, suspension, up to termination of employment or volunteer, intern, contractor status with Curative. Additional civil, criminal, and equitable remedies may apply.

9. DOCUMENTATION

N/A

10. REFERENCE DOCUMENTS AND MATERIALS

N/A

11. COLLABORATING DEPARTMENTS

- Medical and Pharmacy UM Departments

12. DOCUMENT CONTROL

APPROVED BY:		
(Printed Name)	**(Date)**	**(Signature)**

REVISION HISTORY			
Date	**Author**	**Version**	**Comments**
			Initial Version

APPENDICES

Any applicable attachments, resources or other materials should be included as appendices in this section. Label each appendix as follows:

Appendix A: